

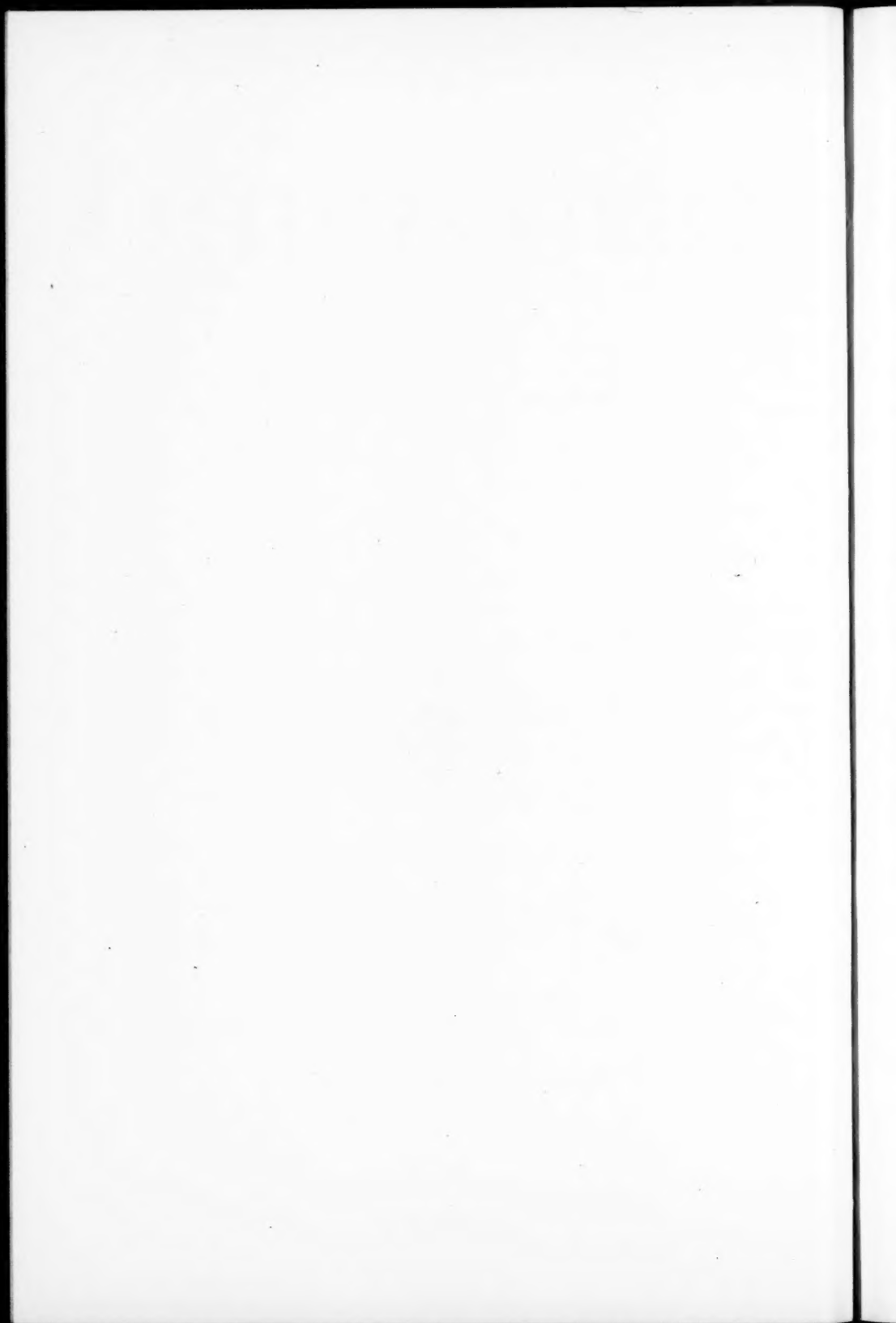
# ANNALS *of* ALLERGY

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VOLUME 2

January through December, 1944



# ANNALS of ALLERGY

## Contents for Volume 2

JANUARY-FEBRUARY, 1944

(Number 1)

THE ART OF INTERPRETING THE PULSE-DIET RECORD IN FAMILIAL NONREAGINIC FOOD ALLERGY. <i>Arthur F. Coca, M.D., F.A.C.A. (Hon.)</i> .....	1
PRACTICAL CONSIDERATIONS OF DEPARTMENTS AS SEEN BY THE ALLERGIST. <i>Philipp Schonwald, M.D., F.A.C.P., F.A.C.A.</i> .....	10
SYRINGE CONTROL IN PASSIVE TRANSFER REACTIONS. <i>Frank A. Simon, M.D., F.A.C.A.</i> .....	15
EVALUATION OF SKIN TESTING IN ALLERGY. <i>James M. Steele, M.D., F.A.C.A.</i> .....	17
CASHEW NUT OIL DERMATITIS. <i>Stephen D. Lockey, M.D., F.A.C.A.</i> .....	22
EDITORIAL: Render unto Caesar.....	26
The Sixth Annual Forum on Allergy.....	28
The Chicago Meeting.....	28
PROGRESS IN ALLERGY: An Index of the Proprietary Drugs and Mixtures Commercially Available for the Symptomatic and Adjuvant Treatment of Bronchial Asthma. <i>Ethan Allan Brown, M.R.C.S. (London), L.R.C.P. (England), F.A.C.A.</i> .....	29
Annual Review of the Recent Literature on Hay Fever. <i>Helen C. Hayden, M.D., F.A.C.A.</i> .....	41
Annual Critical Survey of the Recent Literature on Bronchial Asthma. <i>Leon Unger, M.D., F.A.C.A.</i> .....	49
Abstracts .....	65
GUIDE TO CURRENT LITERATURE ON ALLERGY.....	68
QUESTIONS AND ANSWERS.....	77
CORRESPONDENCE ITEMS .....	78
NEWS ITEMS .....	80
BOOK REVIEWS .....	83

MARCH-APRIL, 1944

(Number 2)

ALLERGIC PULMONARY CONSOLIDATIONS. <i>O. C. Hansen-Pruss, M.D., F.A.C.A., and E. G. Goodman, M.D.</i> .....	85
SKIN REACTIONS TO PATCH TEST WITH HUMAN DANDER. <i>Frank A. Simon, M.D., F.A.C.A.</i> .....	109
FOOD ALLERGY. THE ROLE OF FOOD ALLERGY IN INTERNAL MEDICINE. <i>Herbert J. Rinkel, M.D., F.A.C.A.</i> .....	115
SENSITIVITY TO MINOR POLLENS. <i>Harry L. Rogers, M.D., F.A.C.A.</i> .....	125

## CONTENTS FOR VOLUME 2

PRELIMINARY PROGRAM—FIRST ANNUAL MEETING—AMERICAN COLLEGE OF ALLERGISTS .....	129
THE MOLAR STANDARDIZATION OF RAGWEED POLLEN EXTRACTS. <i>George E. Rockwell, M.D., F.A.C.A.</i> .....	137
STERILE ABSCESS COMPLICATING ALUM-PRECIPIATED TETANUS TOXOID. <i>Arnold J. Rawson, Assistant Surgeon (R), U.S.P.H.S.</i> .....	145
PHOTOGRAPH—French K. Hansel, M.D., President, American College of Allergists	150
EDITORIAL:	
The Annual Meeting .....	151
Our Guest Speaker.....	153
Veterinary Allergy .....	155
PROGRESS IN ALLERGY	
The Vitamins and Allergy. <i>Ethan Allan Brown, M.R.C.S. (London), L.R.C.P., (England), F.A.C.A.</i> ....	156
Allergy in Otolaryngology and Ophthalmology. <i>French K. Hansel, M.D., F.A.C.A.</i> .....	165
GUIDE TO CURRENT LITERATURE ON ALLERGY.....	173
CORRESPONDENCE ITEMS .....	183
IN MEMORIAM .....	184
NEWS ITEMS .....	186
BOOK REVIEW .....	187

## MAY-JUNE, 1944

### (Number 3)

ALLERGY OF THE CENTRAL NERVOUS SYSTEM. <i>T. Wood Clarke, M.D., F.A.C.A.</i> .....	189
ETIOLOGY OF SEASONAL HAY FEVER IN THE DISTRICT OF COLUMBIA. <i>Grafton Tyler Brown, M.D., F.A.C.A.</i> .....	197
THE PRESENCE OF THERMOSTABLE INHIBITING FACTOR IN THE SERA OF PATIENTS TREATED FOR HAY FEVER BY INJECTIONS OF POLLEN EXTRACT. <i>Ethan Allan Brown, M.R.C.S. (London), L.R.C.P. (England), F.A.C.A., and Captain Eugene M. Holden, M.C., U.S.A.</i> .....	207
SYMPATHECTOMY AS AN AID IN THE RELIEF OF FAMILIAL NONREAGINIC FOOD ALLERGY. <i>Arthur F. Coca, M.D., F.A.C.A. (Hon.)</i> .....	213
THE PROTECTION OF THE ASTHMATIC PATIENT AGAINST LUNG IRRITANTS. <i>Karl J. Deissler, M.D., F.A.C.A.</i> .....	225
AN UNUSUAL CASE OF SULFATHIAZOLE SENSITIVITY OF THE RENAL TYPE. <i>John Peters, M.D., F.A.C.A., and Arthur J. Koven, M.D.</i> .....	230
THE IMPORTANCE OF VITAMIN C IN BODILY DEFENSES. <i>Louis Pelnor, M.D.</i> .....	231
EDITORIAL:	
The Chicago Meeting .....	233
PROGRESS IN ALLERGY:	
Insects and Allergy. <i>Ethan Allan Brown, M.R.C.S. (London), L.R.C.P. (England), F.A.C.A.</i> ....	235
Eczema—Allergic Dermatitis. <i>Stephan Epstein, M.D.</i> .....	247
GUIDE TO CURRENT LITERATURE ON ALLERGY.....	267
NEWS ITEMS .....	277
BOOK REVIEW .....	279



## CONTENTS FOR VOLUME 2

### JULY-AUGUST, 1944

#### (Number 4)

QUALITATIVE DIFFERENCES AMONG CANINE DANDERS. <i>Sanford B. Hooker, M.D., F.A.C.A. (Hon.)</i> .....	281
HISTOPATHOLOGY OF ECZEMATOID DERMATOSES. <i>Wilbert Sachs, M.D., Charles S. Miller, M.D., and Margaret Gray, B.A.</i> ....	289
PRECIPITATION OF PULMONARY EDEMA BY AN OVERDOSE OF ANTIGEN IN A PATIENT WITH RHEUMATIC MITRAL DISEASE. <i>Karl J. Deissler, M.D., F.A.C.A.</i> .....	299
PSYCHIATRIC STUDIES IN CLINICAL ALLERGY. <i>Ethan Allan Brown, M.R.C.S. (London), L.R.C.P. (England), F.A.C.A., and P. Lionel Goitein, D.P.M., M.B., B.S. (London)</i> .....	303
POLLINATION OF ANEMOPHILOUS TREES IN NEW ORLEANS. <i>Wm. T. Penfound, Ph.D.</i> .....	315
SEVERE URTICARIAL REACTIONS DUE TO POOLED HUMAN PLASMA. <i>Captain Bernard Dickstein, M.C., A.U.S., F.A.C.A.</i> .....	327
CONTACT DERMATITIS FROM RUBBER GAS MASK. <i>Captain Joe C. Gilbert, M.C., A.U.S.</i> .....	339
SUBCUTANEOUS EMPHYSEMA DURING ASTHMA. <i>Nathan Francis, M.D., F.A.C.A.</i> .....	342
LOCALIZED ATROPHY OF THE SUBCUTANEOUS FAT AFTER REPEATED INJECTIONS OF GRASS POLLEN. <i>Nathan Francis, M.D., F.A.C.A.</i> .....	344
EDITORIAL: Instructional Course .....	346
The Standardization Committee.....	348
Microfilm of Army Medical Literature Readily Available.....	348
PROGRESS IN ALLERGY: Immunology in 1943. <i>A. J. Weil, M.D., F.A.C.A.</i> .....	349
NEWS ITEMS .....	359
BOOK REVIEWS .....	362

### SEPTEMBER-OCTOBER, 1944

#### (Number 5)

ARMY ALLERGY—FOURTH SERVICE COMMAND 1943. <i>Colonel Sanford W. French, MC, USA and Major Lawrence J. Halpin, MC, AUS</i> .....	365
ALLERGIC SKIN DISEASES IN THE NAVY. <i>Comdr. Marion B. Sulzberger, MC, USNR</i> .....	380
ALLERGIC OCCUPATIONAL DERMATITIS IN OUR WAR INDUSTRIES. <i>Louis Schwartz, M.D., F.A.C.A. (Hon.)</i> .....	387
ALLERGY IN RELATION TO THE GENITO-URINARY TRACT. <i>J. Warrick Thomas, M.D., F.A.C.A., and Vernon P. Wicksten, M.D., F.A.C.A.</i>	396
CLINICAL EVALUATION OF SOYBEAN FOOD IN ECZEMA OF THE CHILD. <i>Albert V. Stoesser, M.D., F.A.C.A. (Associate)</i> .....	404
THE ALLERGIC PROBLEM OF THE INDUCTEE, THE SOLDIER AND THE VETERAN. <i>Captain Henry I. Shanon, MC, AUS</i> .....	413
EXPERIMENTAL APPROACH TO ORAL TREATMENT OF FOOD ALLERGY. <i>Erich Urbach, M.D., F.A.C.A.; George Jaggard, B.S., F.A.C.A. (Associate), David W. Crisman, V.M.D., F.A.C.A. (Associate)</i> .....	424
ALLERGY IN MEXICO. <i>Mario Salazar Mallén, M.D., F.A.C.A. (Hon.)</i> .....	433

## CONTENTS FOR VOLUME 2

EDITORIAL:	
Old Age Security.....	438
Research Fellowships Available in Consideration of Standardization of Allergic Extracts .....	438
PROGRESS IN ALLERGY:	
Pediatric Allergy.....	
Jerome Glaser, M.D., F.A.A.P., F.A.C.A.....	440
NEWS ITEMS .....	453
BOOK REVIEWS .....	454

## NOVEMBER-DECEMBER, 1944

### (Number 6)

THE MECHANISM OF ANAPHYLACTIC AND ALLERGIC REACTIONS. An Evaluation of the Role of Histamine in Their Production.	
Charles F. Code, M.D., F.A.C.A.....	457
THE MECHANISM OF DESENSITIZATION.	
J. Bronfenbrenner, Ph.D., F.A.C.A. (Hon.).....	472
MOLD FUNGI IN THE ETIOLOGY OF RESPIRATORY ALLERGIC DISEASES.	
III. Immunological Studies with Mold Extracts.	
1. Preparation of Experimental Extracts.	
Homer E. Prince, M.D., F.A.C.A., and Marie B. Morrow, Ph.D.....	483
2. Skin Tests with Experimental Extracts.	
Karl D. Figley, M.D., F. W. Wittich, M.D., F.A.C.A., J. H. Black, M.D., Paul T. Petit, M.D., F.A.C.A., Erle D. Sellers, M.D., F.A.C.A., James A. Mansmann, M.D., F.A.C.A., and Homer E. Prince, M.D., F.A.C.A.....	489
3. Failure to Find Histamine-Like Substances in the Washings and Extracts of Molds Used for Skin Testing.	
W. A. Selle, Ph.D.....	493
4. Skin Tests with Broth and Washings from Mold Pellicles.	
Homer E. Prince, M.D., F.A.C.A.....	500
MOLD FUNGI IN THE ETIOLOGY OF RESPIRATORY ALLERGIC DISEASES.	
IV. Skin Reactions to Mold as Correlated with Relative Importance in Treatment.	
Pearl L. Zink, M.D., F.A.C.A.....	502
FOOD ALLERGY.	
II. The Technique and Clinical Application of Individual Food Tests.	
Herbert J. Rinkel, M.D., F.A.C.A.....	504
THE INFLUENCE OF HYPNOSIS ON PASSIVE TRANSFER AND SKIN TESTS.	
Michael Zeller, M.D., F.A.C.A.....	515
EDITORIAL:	
Mayo Clinic Fellowship.....	518
The St. Louis Graduate Instructional Course.....	518
The Index Number—An Appreciation.....	519
The Seventh Annual Forum on Allergy.....	519
NEWS ITEMS .....	521
IN MEMORIAM .....	523
BOOK REVIEWS .....	524
INDEX TO VOLUME 2.....	525

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# ANNALS *of* ALLERGY

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Volume 2

January-February, 1944

Number 1

## **THE ART OF INTERPRETING THE PULSE-DIET RECORD IN FAMILIAL NONREAGINIC FOOD ALLERGY**

**ARTHUR F. COCA, M.D., F.A.C.A. (Hon.)**

**Pearl River, New York**

**T**HE specific treatment of the numerous manifestations of familial non-reaginic food allergy, as previously described,<sup>1,2</sup> is based on the principle that the ingestion or inhalation of the allergenic substance regularly causes acceleration of the pulse rate. This specific acceleration varies in extent up to a maxima of 30 beats or more per minute above the normal maximum for the individual, and it usually occurs within one hour after ingestion of the allergenic food.

This specific effect of nonreaginic food allergy has been observed in all cases thus far studied with this criterion, even in food-allergic persons who have not yet begun to experience any other allergic symptom. Thus, this criterion is one of the most dependable in the field of human pathology; as dependable, in fact, as the recently reported physiological constant of the individual normal pulse rate.<sup>3</sup>

It was proper, in the first reports concerning the treatment, to give prominence to the typical, uncomplicated cases illustrating this phenomenon; although it was pointed out that frequent difficulties of interpretation of the pulse-diet record arise which are caused by several apparent exceptions to the above-mentioned rule.

The apparent exceptions referred to have been previously discussed; they are the "recurrent" reaction, the "latent period" of temporarily lost sensitivity after more or less prolonged avoidance of the allergen, the delayed reaction, the emergence of sensitivity to minor allergens, and the depression of the reactivity of the shock tissues by allergic insults.

The recurrent reaction ("carry-over") is illustrated in the charts of the pulse records of M. M. D., A. R., J. G., and C. T., in the earlier reports.<sup>1,2</sup> Evidently the pulse-accelerating effect of an allergenic food may be partly or entirely obscured if contact with the food is had at the time of a carry-over from another allergen. Also, a series of strong

From Lederle Laboratories, Pearl River, New York.

# PULSE-DIET RECORD—COCA

TABLE I

Date December 8	9	10	11	12	16	18
Pulse						
B. R.— . 60	. 61	. 56	. 56	. 59	. 56	. 64
Br. . 63	. 55	. 57	. 67	. 65	. 62	. 65
30' . 77	. 75	. 72	. 79	. 66	. 68	. 66
60' . 90	. 83	. 81	. 75	. 68	. 66	. 65
90' . 85	. 88	. 88	. 68	. 69	. 65	. 62
Diet Oatmeal	orange EGGS	EGGS milk	EGGS milk	banana milk	Cream of Wheat, ham toast, milk	prunes sugar cornflakes milk
Mid.						
A. M. . *	. 77	. 79	. 62	.	. 67	. 63
30' . 74	. 83	. 81	. 64	.	. 69	. 67
60' . 79	. 79	. 87	. 65	.	. 71	. 68
90' . 75	. 72	. 76	. 62	.	. 70	. 68
Diet milk	carrot	tomato	tomato		grapes	tangerines
Lunch . *	. 65	. 85	. 55	. 60	. 68	. 64
30' . 68	. 76	. 90	. 68	. 63	. 71	. 66
60' . 70	. 86	. 88	. 62	. 57	. 67	. 64
90' . 73	. 84	. 88	. 59	. 63	. 64	. 63
Diet EGGS	beef	fish STRING BEANS cole-slaw milk	salmon milk	carrot banana Junket	lamb chops milk	lamb chops milk
Mid.						
P. M. . *	.	. 88	. 62	.	. 68	.
30' . 86	.	. 80	. 59	.	. 70	.
60' . 88	.	. 77	. 57	.	. 71	.
90' . 76	.	. 78	. 59	.	. 69	.
Diet apple		grapes	banana		orange banana	
Dinner . *	. 69	. 65	. 60	. 64	. 62	. 69
30' . 62	. 73	. 61	. 61	. 63	. 66	. 71
60' . 67	. 77	. 68	. 63	. 64	. 68	. 63
90' . 64	. 69	. 72	. 64	. 65	. 67	. 67
Diet chicken	chicken potato milk	chicken milk	lamb chop fried potatoes milk	tomato chicken potato PEAS, milk	creamed beef spinach milk Junket	hamburger macaroni PEAS (few) milk
Ret. . *	. 61	. 65	. 55	. 65	. 56	. 57

\*Count omitted by mistake. B. R.—before rising.

Name: W. R. (chief symptom—convulsive seizures at 3-week intervals).

allergic reactions, sometimes even a single one, may so depress the shock tissue that a further exposure to the same or another allergen may fail to elicit more than a slight reaction. Finally, a carry-over effect may be mistaken for a reaction to a new food to which the patient is not allergic.

These difficulties are especially disturbing if they present themselves at the outset of the treatment as some of them, with others, did in W. R., a part of whose pulse-diet record is shown in Table I.

#### PULSE-DIET RECORD—COCA

On the two days just preceding the first day (December 8) of the trial diet the patient had eaten repeatedly two of his major allergens (egg, bean). Although he had eaten nothing since lunch on December 7, there was a marked acceleration of the pulse (carry-over) after his breakfast of oatmeal, to which he is not allergic (see negative tests with wheat, cane sugar and corn on December 16 and 18, which, in my experience, exclude sensitivity to cereals).

Accepting 60 as the normal low rate in this case, a rate of 73 at ninety minutes after eating egg seemed nonallergic. However, the omitted count just before eating apple might well have been high (thus warning against egg), because at a later test with two apples the pulse rate did not rise above 66; hence, the much higher rates recorded after the mid-P. M. apple of December 8 were probably due to the eggs. In the circumstances, egg was not suspected and was eaten again on the next morning with orange—a new test. The resulting rise of the pulse rate was attributed to orange, and eggs were eaten again the next two days.

At this time it was seen that the normal low rate was not 60 but 55-56, which indicated a normal high point not over 70. Thus, the 79 after eggs on the morning of December 11 was recognized as allergic and eggs could be suspected and eliminated.

In the meantime, carrot, beef and tomato had come under suspicion but retests of these proved them all to be nonallergenic (see tests of December 12, 16 and 18).

A most important lesson evident in this case is that while tentative guesses must be made as early as possible and *acted upon*, the *final* decisions must await a sufficient experience with the effects of single foods upon the pulse of the particular individual and especially the revelation of his normal pulse range. It frequently happens that this important constant cannot be ascertained until several days or longer after the trial diet has been started. Rinkel<sup>4</sup> has reported carry-overs (from a single test, if I did not misunderstand him) lasting as long as four or even five days. I have frequently observed a similar effect on the pulse rate lasting three days. The difficulties of interpretation under such a circumstance are easily comprehensible.

Another difficulty was encountered in the case of W. R., that is, a delayed reaction to pea. At his first eating of peas, December 12, there was no immediate effect on the pulse rate, but a marked delayed effect, without other symptom, in the morning of the 13th, to a maximum of 93, lasting through the lunch period on a nonallergenic diet. At the second eating of peas, on the 18th, there was again no immediate effect but there was a seizure at 2:15 A. M. on the 19th, with a pulse rate of 92, and a second seizure at 10:00 A. M., with a pulse rate of 100.

From December 11 the dietary solution of the case seemed assured, but for some as yet unexplained reason the patient, after a series of

# PULSE-DIET RECORD—COCA

TABLE II

Date	June 8	9	12	13	14	15	16
	Pulse						
B. R.—	. 66	. 66	. 66	. 68	. 68	. 68	. 66
Br.—	. 66	. 68	. —	. —	. 74	. 72	. 72
	. 74	. 68	. 72	. 74	. 74	. 74	. 74
	. 74	. 68	. 72	. 74	. 74	. 78	. 74
	. 72	. —	. 72	. 78	. 76	. 76	. 74
Diet	oatmeal	coffee	bacon	toast	orange	toast	toast
	cane sugar	cream	coffee	coffee	coffee	butter	butter
(headache)		sugar	toast, milk	milk	sugar	coffee, cream	orange
			sugar	sugar	toast, butte	sugar	coffee
							sugar, milk
Mid.							
A. M.	. 72	.	.	.	. —	.	.
	. 72	.	.	.	. 78	.	.
	. 70	.	.	.	. 76	.	.
	. 70	.	.	.	. —	.	.
Diet	milk				milk		
Lunch	. 72	. 74	. —	. 78	. 78	. 76	. 74
	. 80	. 74	. 78	. 78	. 76	. 80	. 76
	. 90	. 74	. 76	. 78	. 76	. 76	. —
	. 84	. 74	. 76	. 78	. 80	. 78	. —
Diet	EGGS	beef	milk	pork	pork	bacon	beef, rice
		rice, butter		potatoes	rice	milk	string beans
		coffee		string beans	string beans	bread	bread
		cream		tea, sugar	bread	butter	butter
		sugar		bread	butter	Jello, cream	milk
Mid.							
P. M.	.	. 74	.	.	.	.	.
	.	. 74	.	.	.	.	.
	.	. 76	.	.	.	.	.
	.	. 76	.	.	.	.	.
Diet		grapefruit					
		sugar					
Dinner	. 74	. 76	. —	. 72	. 76	. 76	. —
	. 80	. 76	. 76	. 74	. 76	. 76	. —
	. 80	. 72	. 76	. 74	. 76	. —	. —
	. 78	. 72	. 76	. 78	. 74	. —	. 76
Diet	chicken	chicken	pork	ham	pork, rice	beef, rice	chicken
	rice	peas, string	potato	mustard	green beans	string beans	potato
	butter	beans, rice	string beans	coffee	tomato	asparagus	beans
	milk	butter, milk	bread, coffee	bread	bread, butter	bread	tea, lemon
			milk, sugar	sugar		butter	sugar
							bread, butter
Ret.	. 68	(well). 70	. 76	. 78	. 72	. 68	. —

Name: Mrs. M. G. (aged twenty-six).

deliberate violations of the dietary restrictions followed by seizures, was withdrawn from observation.

The record of W. R. illustrates the advantage, which is frequently experienced, in depending upon the criterion of specific acceleration of the pulse rather than upon the occurrence of other symptoms in identifying the allergenic foods.



#### PULSE-DIET RECORD—COCA

This point is illustrated also in the record of Mrs. M. G. (Table II), whose chief food-allergic symptom was recurrent severe headache and whose only food allergen is egg. This patient had been eating egg daily up to and including June 7. The single test on the 8th caused a significant acceleration of the pulse rate but no headache. After a day of abstinence from egg (June 9) a moderate exposure to that food on the 10th (roll glazed probably with egg white) was again followed by tachycardia (96) accompanied with headache.

The elevated blood pressure, 142/90, dropped in two days to 118/74. Egg has been avoided since June 10 and there has been no recurrence of headache.

As has been explained in the foregoing illustrations and by inference in the earlier reports, the allergenic foods and inhalant allergens are regularly identified through the criterion of specific acceleration of the pulse. Exceptionally, the occurrence of other allergic symptoms is helpful when the meaning of the pulse record is not clear. An instance of this fact is seen in the record of Miss A. C. M. (Table III), whose chief symptoms were migraine (left) with vomiting, marked tiredness and constipation; there was also chronic rhinitis, neuralgia and occasional dizziness. The allergenic foods in this case are cereals, cane sugar, citrus fruits, beef, lamb, fish, cow's milk and yeast.

On a mixed diet on February 14, the maximal pulse rate was 100, ninety minutes after dinner. The abnormally low rate of 62 before rising on the 15th seemed to indicate a rapid recovery from the allergic reaction of the previous day, but although the bad headache and nausea beginning about a half hour after the taking of milk was thought to be possibly due to milk, there was no confirmation of this idea in the *lessening* pulse rate. On the 16th, vomiting again followed the ingestion of milk but again with no very impressive tachycardia, due perhaps to the previous eating of the minor allergen grapefruit. It was an unfortunate accident that the patient was allergic to four of the foods eaten on that day.

Since my personal experience had shown that most persons who are nonreaginically allergic to cow's milk can tolerate goat's milk, it was decided to try goat's milk in the hope of providing one nonallergenic food on which the patient could subsist while the systematic search for others could be pursued.

Luckily, goat's milk was tolerated and, as is seen in the subsequent record, the plan was successful. Lamb, carrot, beef and potato were all under suspicion on the 17th but carrot was cleared on the 18th, as also egg. Apple and fish were suspected on the 18th along with potato. The test with oat and cane sugar on the 19th turned definitely against these and this was amply confirmed later. Tomato seemed clear on the 19th (confirmed on the 20th) but lamb, with potato, followed, rather late, by a pulse of 88, seemed still suspect. Ham, potato and apple

## PULSE-DIET RECORD—COCA

TABLE III

Date	Feb. 15	16	17	18	19	20	21
	Pulse	(vomited)					
B. R.	62	68	70	68	68	64	66
Br.	68	70	76	72	74	72	74
	76	86	72	76	84	80	70
	84	84	80	76	82	78	68
	80	84	75	80	80	74	70
Diet	OATMEAL	GRAPE-FRUIT	goat's milk	goat's milk	OATMEAL SUGAR goat's milk ("feeling sick at stomach")	goat's milk (feels well)	goat's milk
Mid.							
A. M.	84	80	86	72	70	74	74
headache	80	84	84	72	80	74	80
nausea	72	88	77	72	76	74	76
	80	82	76	72	72	76	72
Diet	MILK	MILK (vomited)	goat's milk (no nausea today)	carrot	tomato	tomato	tomato lettuce
Lunch	72	80	80	76	72	80	72
	84	80	86	76	80	88	74
	80	80	84	80	78	88	84
	80	88	84	76	80	78	80
Diet	eggs (vomited)	LAMB chop	LAMB chop	egg	LAMB chop potato	BEEF potato	ham potato (walking)
Mid.							
P. M.	84	96	76	80	.	78	80
	88	96	85	78	.	80	80
	80	84	78	78	.	76	76
	88	78	76	84	.	74	72
Diet	apple (vomited)	ORANGE	carrot	apple	.	carrot	banana
Dinner	.	84	88	88	88	78	76
	.	80	84	88	80	80	84
	.	92	88	84	80	76	80
	.	96	96	76	80	84	80
Diet	no dinner (vomited)	chicken	BEEF potato	FLOUNDER potato	ham carrot potato apple	ham potato apple	ham, egg potato goat's milk apple
Ret.	90	75	96	72	74	76	78

Name: Miss A. C. M. (aged fifty)  
Advised Vitamin B Complex, 4 caps. daily.

looked safe at dinner on the 19th. Beef was suspected at lunch on the 20th (no later test). After the clearing of potato, beef and lamb were placed definitely on the forbidden list. All foods eaten on the 21st were considered safe, the two rates of 84 being considered a carry-over effect.

The moderate acceleration of the pulse (84) after dinner on the 22nd was believed to be due to the fish, although apple had not been definitely

## PULSE-DIET RECORD—COCA

TABLE III—Continued

Date	Feb. 22	23	24	25	26	27	28
Pulse							
B. R.	70	68	66	66	66	64	68
Br.	72	75	72	70	70	68	72
slight	76	80	86	80	80	76	72
headache	80	80	80	80	76	76	76
	80	82	80	78	76	76	76
Diet	goat's milk	goat's milk banana	goat's milk dates	goat's milk dates	prunes beet sugar goat's milk	prunes goat's milk beet sugar	prunes goat's milk beet sugar
Mid.							
A. M.	72	72	70	68	72	76	76
	72	76	76	72	72	72	76
	70	74	72	72	72	68	72
	68	76	72	72	74	68	72
Diet	tomato	tomato	tomato	tomato	tomato	tomato	tomato
Lunch	68	84	72	72	74	76	76
	76	88	80	80	82	80	76
	76	80	76	80	80	76	76
	76	80	72	72	76	76	72
Diet	eggs potato	ham egg potato	eggs carrot white potato goat's milk	eggs white potato carrots goat's milk	boiled eggs potato carrots (restaurant)	eggs potato carrots goat's milk	eggs baked sweet potato carrots
Mid.							
P. M.	80	80	70	72	72	76	72
	76	80	76	72	76	76	76
	72	72	76	72	76	76	76
	72		76	72	72	72	76
Diet	banana	banana	dates	dates	raw prunes	raw apple	raw apple
Dinner	80	80	78	76	76	76	80
	84	82	80	80	80	80	80
	84	84	80	80	72	76	76
	84	80	80	72	72	72	72
Diet	<b>FLOUNDER</b> potato carrot apple beet sugar	<b>SALMON</b> potato carrot goat's milk	eggs peas potato goat's milk	eggs white potato carrots peas butter	eggs potato string beans peas goat's milk	eggs string beans white potato spinach goat's milk	eggs white potato string beans spinach
Ret.	72	75	72	72	76	78	76

Name: Miss A. C. M.

cleared and beet sugar was being eaten for the first time. The two rapid rates (84 and 88) at lunch on the 23rd were almost certainly a carry-over effect from the previous evening. The rates of 82 and 84 after dinner were believed to be caused by the salmon and the acceleration (86) after breakfast on the 24th was interpreted as carry-over.

Subsequent tests of new foods were undertaken cautiously for two reasons. The most cogent of these was the very severe, prolonged symptoms (vomiting, migraine) that followed the tests with cow's milk and that had to be feared as possible consequences of tests with other allergens. Another consideration was the importance of convincing the

#### PULSE-DIET RECORD—COCA

patient early of the dependability of the pulse rate as a criterion of allergenic and nonallergenic foods; a number of symptomless days in succession constantly associated with a normal pulse range (64 to 80 in this case) usually suffices for this purpose.

One is reminded here of the fact that the success of the specific treatment of nonreaginic food allergy depends largely upon the coöperation of the patient and his understanding of the theoretical basis of the treatment.

The subsequent course was uneventful. Five months later the patient reported that she had lost a total of  $9\frac{1}{2}$  pounds of excessive weight. Four and one-half pounds had been lost in the first week (probably water of edema) and another three pounds gradually in the next four weeks. She was free of fatigue, constipation, headaches and the chronic rhinitis. Her constantly split fingernails were healed. Her daily pulse range was 64 to 80. Final weight  $129\frac{1}{2}$  pounds.

It is apparent that the solution of the succession of problems of interpretation presented in these cases was arrived at on the basis of the primary assumption that *all variations from the normal, both in the pulse record and in the record of the other symptomatology, were specific allergic effects*. The anxious eight-year search for a serious fallacy in this assumption has not revealed one such.

There are practical difficulties in the management of nonreaginic food-allergic patients besides those of interpretation of the pulse record. By all odds, the most disturbing of these is in the identification and avoidance of nonreaginic *inhalant* allergens.

Nonreaginic sensitivity to house dust can sometimes be recognized when the pulse rate before rising is consistently higher than the rate on retiring. However, the effect of the mattress and pillow dust on the pulse may not be apparent until shortly *after* rising.

Nonreaginic sensitivity to tobacco, which is not infrequent, can easily be detected by having the patient smoke between meals (conveniently in the evening) at a time when the pulse rate is within the normal range. The resulting acceleration of the pulse in the tobacco-sensitive person has usually begun within fifteen minutes. It had not occurred to the author to make such a test with nonsmokers until relatively recently, when several nonsmoking patients were accidentally found to experience nondietary tachycardia and other allergic symptoms—elevation of blood-pressure, indigestion, neuralgia—after exposure to the tobacco smoke of others.

Other elusive inhalant allergens, the presence of which in one's immediate environment in effective quantity cannot always be detected by the patient, are cosmetic powders, perfumes, coal gas, soap powders, automobile exhaust fumes.

Unfortunately, the nonreaginic sensitivity to the inhalant allergens is at

## PULSE-DIET RECORD—COCA

least often not extinguished by the operation of sympathectomy, which will be the subject of a later report.

Incidentally, it should be pointed out that the plan of application of the trial diet in the three cited cases is different from that indicated in the earlier monographic report.<sup>2</sup> The five "meals" of the first day are all of one food each.\* In some instances it is advantageous to repeat this program on the second day, thus getting further away from the allergic effects of the last days of unrestricted diet.

### SUMMARY

Some of the difficulties of interpreting the pulse-diet record in the practical management of familial nonreaginic food allergy are illustrated in a few cases and suitable means of overcoming them are discussed.

The case records indicate the manner in which the trial diet is now being applied by the author.

### SUMARIO

Algunas de las dificultades de la interpretación del record del pulso en el manejo práctico de la familia no-reagínica a la alergia alimenticia se presentan en unos pocos casos y los medios apropiados para salvarlas son presentados.

Los casos registrados indican la manera en la cual la "dieta de prueba" esta siendo aplicada ahora por el autor.

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\*In the earlier program, two foods were given at some meals with the idea that the patients might object to greater restriction. However, experience has taught that most sufferers from food-allergy who seek medical aid will submit to any restriction that seems to promise relief. Evidently the result of a test with a single food will often be less equivocal than one with two foods.

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The seeds of the white lupine of Europe (*Lupinus Albus*), used as a food from earliest times, has by plant breeding been developed into a sweet palatable food in Russia and Germany. The protein from these seeds has a nutritional value next to soybeans.

## PRACTICAL CONSIDERATIONS OF DERMATOPHYTOSES, AS SEEN BY THE ALLERGIST

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IN the last few years the public has become food-allergy conscious and has also been aware of food allergy as a cause of skin eruptions. This tends to bring an ever-increasing number of dermatological conditions to the allergist for diagnosis and treatment. Naturally, only a small number of these self-diagnoses are correct. Careful diagnostic studies reveal the true etiology of these conditions and show that only a limited number of these dermatoses are due to food allergy.

The combined experience of allergists in this country has established a few pertinent facts about the dermatological symptomatology of food allergies which it is well to keep in mind. (1) Food allergy is much more apt to occur in young people, infants, babies, and small children. It is comparatively rare in adults, in whom it takes definitely second place to inhalatory and intrinsic allergy. (2) The sites of skin rashes due to food allergy are characteristic and offer a help in making the diagnosis: these locations are the cubital and popliteal fossæ and the face. (3) Skin lesions due to food allergy are primarily sterile and infection is always secondary.

A great number of the supposedly allergic skin disorders we have seen during the last few years did not at first glance appear to be due to food allergy, because they did not fall in with these just enumerated principles. Most of the patients were adults and the locations of the dermatoses were not typical and they were infected as our routine microscopic examination showed. Furthermore, the majority of these cases proved to be caused or infected by trichophyton and epidermophyton, and it is this important aspect with which this report deals. To review a fair cross-section of this problem, 100 consecutive cases have been picked at random and will be discussed to bring out practical points of diagnosis and treatment. All these cases upon microscopic examination revealed the presence of mycelia and spores of trichophyton or epidermophyton.

Trichophyton gypseum is by far the most common of the species encountered in this country. Other trichophytons like *Tr. violaceum*, *Tr. crateriforme* and *Tr. sulfureum* are rare in the United States. *Tr. purpureum*, which is common in the tropics and in the South, most probably will be seen more often as our soldiers come back from these regions. Trichophyton gypseum can easily be identified under the microscope if a scale of the affected area moistened with a drop of normal 10th hydroxide solution is examined with the high power. The mycelia are septate and branched. Spores are numerous, small and roundish. Fur-

ther characteristics of the microscopic appearance of *Tr. gypsum* are: Mycelia en raquette, nodular organs and spirals. Epidermophyton examined in the same manner is characterized by many large club- or spindle-shaped spores (fuseaux). The culture of *Tr. gypsum* grown on 10 per cent malt-agar is white, while the culture of epidermophyton is of a grayish, olive-drab color.

Another important diagnostic aid is the allergic skin reaction to trichophyton extract. *Tr. gypsum* gives more positive skin reactions to trichophyton than *Tr. purpureum*. That explains why *Tr. gypsum* causes dermatophytids, while the *Tr. purpureum* does not. The latter is more resistant to therapy. People sensitive to one type of trichophyton react also to extracts from other species.

The appearance of these dermatophytoses is protean, and may present an apparently undamaged skin surface as in pruritus or show the well-known pathologic change of a deep-seated, infectious, eczematous dermatitis, as in some cases of long standing and bacterial mixed infection. Often the examination of a slide is not sufficient and it is necessary to culture a specimen on a mold plate or in broth in order to have full information on the invading organism.

The purely allergic feature of all these conditions is the "trichophytid," a manifestation of sensitivity to the trichophyton fungus. The primary lesion may be small and insignificant but is usually of long standing. The trichophytid often suddenly appears on a remote part of the body and is sterile, but usually soon becomes infected with trichophyton. We have encountered a sterile trichophytid in only twenty-six of these 100 cases, although all the cases who presented a widespread general infestation of almost the whole skin must have been trichophytids at one time. There were 7 such cases.

Peck, in 1929, produced "ids" of the hands by irritating interdigital trichophytosis. In animals "ids" have been produced by injections of trichophytin.

Stokes et al., in a very interesting article on dermatophytosis, emphasize that the interplay of infection and allergy must always be kept in mind, especially in a virus infection which tends to increase the range and seriousness of contact-allergy, ingestant-allergy and inhalant-allergy. In many cases with allergic backgrounds, one witnesses the sudden extension of eruptive manifestations, locally or over the body generally; these extensions are spoken of as "ids," as an expression of the extending, broadening or heightening allergic susceptibility of the individual to his infecting agent. The authors warn against using x-rays in the treatment of mycotic and pyogenic-allergic hand and foot infections as a first and not as a last resort. While x-rays give at the start remarkable relief in a large proportion of cases, it is rare to see a lasting recovery follow roentgen irradiation.

"Ids" will take on different forms and are sometimes difficult to



## DERMATOPHYTOSES—SCHONWALD

recognize as such. Pruritus ani, as Foster and Hill have pointed out, is frequently an "id" resulting from a distant focus of infection, particularly seborrheic eczema and dermatophytosis. We have seen cases of perennial allergic rhinitis of considerable severity which were found to be related to a distant dermatomycosis and cured by hyposensitization with trichophyton extract.

The correct diagnosis of a dermatophytid depends on four minimal obligatory conditions: (1) demonstrable focus, (2) irritation of the primary focus characterized by inflammation, swelling, et cetera; (3) positive trichophyton skin test, (4) usually no fungus is found in the "id" (Lewis and Hopper).

The most frequently encountered locations of the skin disorder were the hands (twenty-five cases) and the face (fifteen cases). The scalp was invaded seven times, the eyebrows four times, the external ear canal five times. The last three mentioned locations seem to present a more difficult problem, apparently due to purely local anatomical conditions. Seventy-nine of these cases were of long standing and nineteen of them had a secondary bacterial infection. Only eight of the cases reported here were nonallergic. Sixty-two patients gave definite skin reactions to trichophyton, sixty-eight reacted to fungi in general, forty-five to pollen, forty were allergic to foods, eleven to dust. Fifty-three of these patients were cured, thirty-eight were controlled. (Most of these were still under treatment at the time of this writing.) Four were complete failures and five were not heard of. It does not seem to make any difference whether the condition is due to trichophyton or epidermophyton, as far as appearance of the lesion or therapy are concerned.

Trichophyton may invade any part of the body surface from the scalp to the toes, while epidermophyton more often is found in eruptions on intertriginous surfaces as on the thighs, the groin, under the axillæ, the mammæ, et cetera.

Local therapy consists of irradiation with the cold quartz lamp, which has definitely more fungicidal power than the (hot) mercury vapor lamp. In the cold quartz lamp Argon and Xenon gases are used to ionize the mercury. Above 90 per cent of the total ultraviolet output of the Rose cold quartz is in the single band of 2536-37 Ångstrom units. Caution must be used with this treatment, seldom more than three to five minute exposures are given.

Ultraviolet irradiation kills the vegetative stage of the dermatophyte, i.e., the mycelia. Spores are more resistant and therefore continuous, and prolonged treatment is necessary to prevent reinfection by the constantly and abundantly produced spores. Fungus spores survive cold, sunshine and other extreme conditions (Goldman). They have been found up to 14 miles in the stratosphere. Only heat (48 centigrades for ten minutes) kills them. This explains also why immunization with trichophytin is the most desirable procedure.



Dead tissue interferes with local treatment and tends to keep the lesions moist. Application of sodium thiosulphate solution (10 per cent or less) promotes scaling and reduces swelling and weeping. The itching is also controlled by application of sodium thiosulphate or ether.

Local application of ointments and salves of any kind is to be avoided as fat seems to favor the growth of these fungi.

In the treatment of cases mixed infected with cocci, (and these are the deep-seated lesions, raw, weeping and painful) we have been using an antibiotic derived from a soil bacillus with remarkable success.

As far as x-ray treatment for these conditions is concerned, this writer agrees wholeheartedly with the opinion of Stokes and his co-workers on this subject, which is mentioned above.

The most important feature of general treatment is hyposensitization with a mixed trichophytin. As early as 1935, Robinson and Grauer reported a series of mycotic infections successfully treated with autogenous extract and recommended this procedure as the treatment of choice for refractory dermatomycoses. Many different types of antibodies have been demonstrated in trichophytin, such as inhibit growth in cultures (Jessner and Hoffman, Ayres and Anderson).

This hyposensitization treatment has its scientific foundation in the importance of the allergic feature of most of these trichophyton infections. The severity of infection depends on many factors but primarily on the allergic response of the individual to the fungus invasion. Henrici points out that the allergic state is definitely responsible for tissue injury and consequent inflammatory reaction in dermatomycoses. The ultimate healing is also due to the allergic state. Guinea pigs show typical allergic behaviour on secondary and later reinfection; by continuous reinoculation the animal becomes immune.

The trichophytin we use is derived from a great number of different strains which we have collected during the last eight years. We begin with a 1:100,000 solution and give injections twice weekly, subcutaneously, slowly increasing the amount until 0.5 c.c. of a 1:100 dilution is reached.

Inasmuch as most of these patients were allergies, their allergies other than to trichophytin had to be given proper consideration. Pollen, mold and dust allergies were treated with the proper extracts and food-allergic patients were put on diets. All these patients were advised to abstain from eating yeast, drinking beer, and to avoid eating fermented foods. Fifty-one of these patients were given synthetic Vitamin B hypodermically, which seemed to improve their general condition. Debilitated and undernourished patients were given an arsenic iron tonic; ten patients with symptoms of the menopause received estrogenic treatment. In four cases, with involvement of most of their skin, the itching and pain which had kept them awake for many nights were alleviated by intravenous injection of aminophylline.

## DERMATOPHYTOSES—SCHONWALD

The incidence of dermatophytosis is much higher than is generally known. It is estimated by various authors to be 37 to 89 per cent of the total population. Hulsey and Jordan, on microscopic examination of students, found 63 per cent to be affected.

Wise and Wolf state the incidence of superficial mycotic lesions is very widespread all over the world. They distinguish (1) superficial dermatomycoses, due to trichophyton, epidermophyton or yeasts; (2) eruptions of secondary nature (ids); (3) eruptions caused by exogenous irritants (dermatitis venenata), occupational dermatoses; (4) eruptions due to food and drug allergy.

Cleaning fresh vegetables and working in the soil has been responsible for many an outbreak of dermatophytosis. Most of our patients were definitely allergic to fungi and soil molds, mainly *Hormodendron* and *Trichoderma*. These seem to cause dermatoses which then become infected with dermatophytes. The victory garden movement which induced many more people to work in the soil is responsible for a greater incidence of these conditions, especially on the hands. The use of rubber gloves is not advisable, as they cause perspiration and moisture of the skin and thereby create conditions favorable to the growth of fungi. Anything that causes maceration of skin favors the infection with fungi which exist and grow only in dead tissues.

### SUMMARY

A review of 100 consecutive cases of dermatophytosis is presented and the allergic phase of this condition discussed. Practical viewpoints as to diagnosis and treatment are offered.

### SUMARIO

Un examen de 100 casos consecutivos de dermatofitosis es presentado y la falsa alérgica de esta condición presentada.

Prácticos puntos de vista concernientes a diagnosis y tratamiento son presentados.

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## SYRINGE CONTROL IN PASSIVE TRANSFER REACTIONS

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THE local passive transfer reaction is more convincing evidence of the existence of hypersensitiveness than the direct skin reaction on the patient because of the more nearly perfect controls which it affords. These controls are:

1. *The Transfer Control.*—This consists of an injection of the allergenic extract into a skin site not previously sensitized with the reagin-bearing serum. This may be a normal skin site or preferably one previously injected with the serum of a nonsensitive individual. The injection must be of the same volume, from the same syringe and made at approximately the same time as that for the sensitized site. A positive reaction in the sensitized site as compared with a negative reaction in this control site proves that something has been transferred, that the donor is sensitive, that his serum contains reagins.

2. *The Specificity Control.*—This consists of an injection of extracting fluid or of some allergenic extract other than the one under investigation into a sensitized skin site. The purpose of this control is to produce the same small "mechanical" wheal in this control site as in other sensitized sites for purpose of comparison and also to prove that the mere injection of fluid or of some other allergen into the sensitized skin site will not produce a positive reaction.

3. *The Syringe Control.*—In addition to the above-mentioned controls, the importance of which is generally recognized at present, a syringe control has been found to be necessary. This is concerned with the problem of syringe contamination, which has been reported by several authors.<sup>1,2,3,4,5,6,7,8,10</sup> In a recent study involving local passive transfer reactions it was observed that certain sera gave positive reactions when the transfer sites were injected with extracting fluid alone, but that this apparent nonspecific transfer of sensitivity could readily be eliminated by using new, previously unused syringes or by cleansing used syringes thoroughly by some acceptable method.<sup>7,9</sup> Hence it is necessary, in any local passive transfer experiments, to carry out a syringe control. This may be done as follows: After thorough cleansing and sterilization, the syringes, with attached needles, are partially filled with extracting fluid. With the needle end up the plunger is twisted and pushed in and out several times so as to insure intimate contact of the fluid with the ground glass inner surface of the syringe and to insure thorough mixing

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## PASSIVE TRANSFER REACTIONS—SIMON

of the fluid. A small quantity of fluid (0.10 c.c. to 0.20 c.c.) remains in the syringe. Sensitized and nonsensitized skin sites are injected with this fluid. The reactions in both must be equal and negative before the syringe is considered acceptable for use in the experiment. Furthermore, it is acceptable only for transfers involving the serum which has been tested. If some other serum is to be used another syringe control must be carried out.

It is not safe to assume, especially in experimental work, that any given cleansing method has been effective. The specificity control referred to above is not a substitute for the syringe control because, while it may prove that the syringe used for this control contains no detectable allergen, it gives no evidence whatever concerning syringes used for other skin sites.

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### POLLEN ANALYSIS AND PREHISTORY

Edward S. Deeby, Jr., reports in the January, 1944, issue of the *American Scientist*\* a most interesting study of pollen chronology as a method by the ecologist of determining the relation of the organism and environment. The author studied the organic sediments of Connecticut lakes with particular attention to the prehistoric pollens found, pointing out that inland lake deposits yield pollen grains which are the most easily recognized and plentiful of the microfossils, and that the vegetation of the surrounding areas is generally influenced by the quantitative composition of the pollen at various levels in the deposits of a lake or a bog. Although local conditions influence the surrounding region, the majority of herbaceous plants and shrubs occurring near such deposits are insect-pollinated and not borne long distances. Most of the fossil pollen originates from the wind-pollinated forest trees within a several-mile radius.

Thus the sequence of pollen occurrences with climatic changes occurring over extensive areas, regardless of local factors, furnishes a chronologic history of life in terms of its environment.

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## EVALUATION OF SKIN TESTING IN ALLERGY

### A Discussion of Causative Factors in Misleading Reactions

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THE art of allergic investigation, since its appearance as a special branch of medicine, has found itself faced with increasing responsibilities, including the necessity of defending certain positions which it holds. Many clinicians who are not devoting their entire time to the progress of this art fail to appreciate the difficulties encountered in the endeavor to reduce to simplicity the infinite complexities of the human organism's responses to an allergenic substance. It is interesting and challenging to observe a candid clinician's reactions to the report he receives from the allergist in regard to the patient whom he has referred for investigation. If these reports are scanned from his viewpoint, it is understandable that the epithet "skin scratcher" has been hurled so contemptuously our way at times.

Indeed, this very expression indicates the direction of perhaps the greatest misunderstanding, and small wonder that the referring physician fails to evaluate properly the meaning and importance of skin tests when allergists differ so widely in their interpretations. To the skeptical, skin testing seems a semi-cabalistic rite bordering on charlatanism, while to the overzealous advocate, every little variation in a zone of erythema around a point of inoculation has tremendous significance, regardless of the clinical picture. In reality, skin testing is a laboratory procedure, performed *in vivo*, and subject to all the variations that should be expected when the diversity of individuals and their physiological reactions is borne in mind.

All workers in this field must be impressed at an early date with the fact that many skins seem refractory or capricious in their degree of response to protein extracts, even when there is little doubt as to the atopic origin of the presenting symptoms. Skin tests which do not parallel the obvious clinical sensitivities tend to make both physician and patient lose confidence in a very valuable procedure. It is the purpose of this discussion to attempt an explanation and clarification of the mechanisms which appear to underlie these misleading reactions, called for descriptive purposes in this paper "false" skin tests. If the presentation lacks strength due to the absence of specific case histories or lengthy bibliography, the author pleads for indulgence since the exigencies of military service have rendered his case records and references temporarily inaccessible. Indeed, little attempt will be made herein to add to the

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AUTHOR'S NOTE: The opinions and assertions contained herein are the private ones of the writer, and are not to be construed as official or reflecting the views of the Navy Department or Naval service at large.

## SKIN TESTING IN ALLERGY—STEELE

erudition of the trained allergist; it is merely hoped that the concepts as elaborated may assist in describing the vagaries of the wayward skin test to the patient and referring physician, in order that better understanding and coöperation may be obtained from both.

### FALSE SKIN REACTIONS

These misleading or "false" skin tests may be roughly classified in three categories:

1. *False negative reactions*, where every evidence points to the atopic origin of the clinical syndrome, by the fulfillment of many of Rackemann's postulates, and still it is impossible to obtain skin reactions of sufficient magnitude to be of any practical value.

2. *False positive reactions*, in those cases where it seems that every, or at least an inordinate number of inoculations are followed by a wheal or flare reaction.

3. *Mixed types*, where a strongly positive reaction on one day is followed by a minimal or absent reaction to the same allergen on the next day, or vice versa.

As a preliminary to consideration of these types of reactions, it is well to review briefly the nature of the allergic reaction, the pathologic change in which is a local increase in capillary permeability, with extravasation of fluid, the cellular content of which is preponderantly eosinophilic in character. This, as applied to the skin, results characteristically in a wheal surrounded by a flare of erythema; the reaction, wherever it occurs, is regarded as being due to the conflict between antigen and antibody, which is attached to the local tissue cells. It is assumed by Lewis that the trauma of this conflict results in the elaboration of histamine-like substance (H substance), which is the direct agent in production of this pathology. Therefore the three main factors which must be considered are the antigen, the antibody, and the tissue where reaction occurs, or shock tissue.

1. *The antigen*, or invading force. It should be borne in mind that the allergic individual's main point of variation from the normal seems to be the inability of his protective mechanism to differentiate between noxious and innocuous proteins. After a sensitizing exposure, the body develops specific antibodies against these antigenic substances, after which subsequent exposures result in the inevitable conflict, and the patient suffers from the secondary effects of a pointless battle. These antigenic substances may be introduced as inhalants, ingestants, or injectants, and are usually proteins in chemical composition. Drug sensitivities are probably developed through union of the drug with a body protein, to which the body becomes sensitized (the haptene mechanism). Sensitization of the skin to oleagenous or detergent substances to produce dermatitis venenata will be disregarded in this discussion.

2. *The antibody* or defensive force. Antibodies are elaborated by the

body in response to the sensitizing exposure to the antigen. It is characteristic of the immunity mechanism that antibodies should be elaborated in superfluous amounts. The origin of these antibodies is still debatable, but the consensus of opinion is that they are the product of living cells, probably of the reticulo-endothelial system. When the antigenic substance is introduced locally in small amounts, the local reticulo-endothelial cells probably elaborate enough antibodies to take care of the situation, leaving the excess to be attached to local tissue cells, and the whole process is still confined to the original shock tissue at the site of primary inoculation.

However, each repetition of this exposure results in the elaboration of more and more antibodies until, after a variable period of time and number of exposures, these antibodies are absorbed into the circulating body fluids and carried, probably by the globulin fraction of the blood, to become attached to tissue cells at remote points. It is conceivable that the same result would occur earlier if the sensitizing or first subsequent doses were massive, or absorbed directly into the blood stream.

When these specific antibodies gain access to the blood stream, they are known as reagins, and are often demonstrable by the reaction of passive transfer (Prausnitz-Kustner). When one considers the important place that the skin holds in the immunity mechanism of the body, as demonstrated by Besredka, it is easy to understand that specific antibodies diffused throughout the organism would have a special affinity for tissue cells in the skin, and, becoming attached thereto, convert the skin into a potential shock tissue.

Thus time, and possibly other factors, including the more widespread elaboration of antibodies stimulated by repeated exposures to antigen, may convert a local foray in the original shock tissue, to a wide area, armed for "total war," and only awaiting the arrival of the "enemy" at the remote outposts.

3. *The shock tissue* or battleground. As has been previously stated, the primary shock tissue is in most instances the tissue of primary exposure. The antibodies at first elaborated by the local reticulo-endothelial cells remain attached to the tissue cells in that vicinity, and unless more are manufactured, remain attached to those cells, confining the diffusion of H substance and consequent pathology to that area. It is not remarkable, then, that skin tests in such a case should be entirely negative, even though the local exhibition of the offending substance will invariably produce a typical allergic response.

After the stimulating effect of repeated exposures, more and more antibodies are picked up in the serum globulin and conveyed to the remote areas and attached to tissue cells of those areas, notably the skin. Thus all the qualifications of a successful skin test are met, and the tissue only awaits the introduction of the specific antigen to evoke the typical wheal and flare reaction.



## SKIN TESTING IN ALLERGY—STEELE

### FALSE NEGATIVE REACTIONS

False negative skin reactions are certainly attributable in some instances to technical errors. It is elementary knowledge that scratch tests are not as sensitive as intracutaneous tests; where tests are indicated at all, patients who are refractory to scratch testing should be followed up by intracutaneous testing.

Another technical factor responsible for failures is the use of grouped allergenic extracts. It seems obvious that the effect of combining five proteins in one extract is to dilute each active ingredient five times; this may be just enough to convert a minimal into a negative response.

The use of impotent extracts is likewise sometimes responsible. Liquid extracts should be dated upon manufacture and upon receipt, and stored in the refrigerator to delay deterioration. Powdered extracts are relatively stable at room temperatures.

However, there are many cases where technical errors are not operative, and skin tests to suspected material are negative, in spite of a well-established diagnosis of allergy. The allergic diathesis is present, the skin is a potential shock tissue, a potent allergenic substance is introduced, and still there is no response. It is obvious that, barring the presence of some blocking factor, the only missing element for success is the specific antibody. The probabilities are in such a case that the reaction is still confined to the primary shock tissue, the antibodies not having yet been disseminated to the skin. It is a common experience to find negative tests for ragweed pollen in a well-established case of seasonal pollinosis, and upon retesting six to twelve months later, find the same tests positive. In these cases, the topical application of strongly suspected proteins will almost always yield the desired confirmatory evidence. In gastro-intestinal, food, and drug allergies where such a procedure is not practicable, one still has recourse to the more laborious procedures of food diaries and elimination diets.

### FALSE POSITIVE REACTIONS

False positive skin reactions are likewise many times the result of faulty technique. Often a zone of erythema is due to a drop of alcohol inadvertently introduced into the skin. An air bubble injected intracutaneously will often produce a reaction of irritation. Also, one occasionally encounters a vial of extract which consistently yields reactions in nearly everyone tested, due to the presence of an adulterant or deterioration of the product. Needless to say, such a vial should be discarded.

However, there are cases where technical faults can be eliminated as a cause, and still the patient, with or without a well authenticated clinical picture of allergy, seems to react to every scratch of the scarifier or insertion of the needle. In most of these cases the clue lies in the fact that the blank test used as a control is as positive as the others, indicating the presence of dermatographia. It must be remembered that the antigen-antibody reaction is not the only mechanism capable of producing H



## SKIN TESTING IN ALLERGY—STEELE

substance in the skin. A wheal may be produced in any normal subject if the trauma is sufficiently severe, and individuals differ in their responses to slight traumatic stimuli, entirely aside from the allergic aspect.

It must be remembered in this regard that frequently positive tests will appear that seem to have no correlation in the clinical history. These are not necessarily false positives, but may represent old sensitivities, the clinical symptoms of which have disappeared in the primary shock organ, but still persist in the skin. Every allergist has seen individuals who have had no hay fever for years still react strongly to skin tests for pollens.

### MIXED FALSE REACTIONS

These reactions may be due to any of the factors already mentioned. In addition, it would be well to stress the fact that protein extracts are relatively thermo-stable, and that the simple heat sterilization of syringes and needles does not necessarily destroy the activity of vestiges of extract remaining in them. At least some strong reactions which cannot be obtained upon subsequent testing are due to the fact that syringes and needles have not been thoroughly washed in preparation for sterilization. It would also appear that the technique used by some, of using the same needle and syringe throughout a series, with only a quick rinse in sterile water between loadings of extract, could be productive of the same result.

### CONCLUSION

In conclusion, a few suggestions are presented which may be helpful in producing the number of misleading skin tests, or at least in assessing their true importance.

1. Be sure each needle and syringe is clean of foreign proteins, as well as being sterile.
2. Be sure to expel air bubbles from the syringe.
3. Follow up negative skin tests with supplementary procedures where possible (topical application of proteins, leukopenic index, food diaries, and elimination diets). Skin tests should be repeated after a variable interval.
4. Use only one protein to a test; eschew the use of combined extracts.
5. Make sure the extracts are fully potent.
6. Remember that dermatographia is a prevalent condition. Skin testing in a large proportion of urticarias is a useless procedure.
7. Always remember, and try to impress on the patient and referring physician, that skin tests are only a valuable adjunct to the clinical findings, and should not be given undue importance.

### SUMARIO

Los factores que pueden causar reacciones falsas en la piel son presentados.

Las falsas reacciones de la piel son clasificadas en tres categorías.

Finalmente, unas pocas sugerencias útiles para disminuir pruebas erróneas de la piel son presentados.

## CASHEW NUT OIL DERMATITIS

STEPHEN D. LOCKEY, M.D., F.A.C.A.

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**C**ONTACT dermatitis has always been an industrial problem of some magnitude. This form of dermatitis is most often seen among men working with dyes, bakelite, glue, paints, varnishes, solvents, coating compounds, resinous oils, et cetera.

The author was requested to investigate an outbreak of dermatitis which resulted from the handling of so-called H. varnish E. 107 and 612 C. It was revealed that one of the main bases of the varnish was cashew nut oil, which was supposed to be in the varnish in an aldehydic state. According to the manufacturer, the varnish was also subjected to several other chemical processes.

The first outbreak of contact dermatitis occurred among workers who handled the so-called H. varnish E. 107. These men had to dip certain pieces of electrical equipment into this varnish. One group had been working with the varnish for some time, with no untoward results. Suddenly, nine of those who had been handling it, developed contact dermatitis.

The areas involved were the hands, forearms, arms and face. One case manifested a severe reaction involving the entire skin surface, resembling an exfoliative dermatitis. All these men were treated conservatively with various ointments and lotions. They also received desensitization therapy with dilutions of a cashew nut oil extract.

The recovery of the eight men was uneventful. The ninth, who was suffering with the exfoliative type, had a stormy convalescence. He developed severe secondary anemia, hematuria, and extreme prostration, but finally recovered.

Subsequently, all the men were patch tested with samples of varnish from the barrel they were using at the time they developed their skin lesions. They were also tested with varnish that they had previously used without any ill effects, and with an extract of raw cashew nut oil. Seven out of the nine men tested reacted to the raw cashew nut oil and to the varnish which they were using at the time they developed dermatitis, but not to the varnish they had used previously. The other two reacted to the raw cashew nut oil but not to either one of the varnishes. This indicated that in all probability something had happened to the barrel of varnish the men were using at the time they developed contact dermatitis. The probability is that the cashew nut oil was not broken down properly during the process of manufacturing.

As stated before, all of these men except one improved rapidly with treatment. Specific desensitization treatment was given to all of them, with cashew nut oil extract, and several of these men have since handled the varnish with impunity.

## CASHEW NUT OIL DERMATITIS—LOCKEY

The cashew nut oil extract for desensitization treatment was made according to Coca's method for the extraction of allergenic oils; 0.5 c.c. of a 2 per cent solution was given intramuscularly every five days until each individual had received five doses.

All the men were then given a so-called tolerance dose of 0.5 c.c. of a 2 per cent solution every five weeks for three doses. Thus, they were treated over an additional period of fifteen weeks. The total period of treatment was from eighteen to twenty-one weeks. Variation in time was due to the inability of the men to report regularly at the same time for treatment.

The varnish H. E. 107 and 612 C. is extremely penetrating and is very hard to remove from the skin surface. The firm continued to use these types because they possessed certain desirable electrical properties. Evidently the first outbreak of dermatitis was due to the faulty treatment during the process of manufacturing the raw cashew nut oil in one barrel of varnish.

Surprisingly, about one year later, a second outbreak occurred. Seven men were affected this time, but not as severely as were the men in the first outbreak, the lesions being limited to the hands and forearms. This group was likewise tested with the varnish which was being used when the dermatitis occurred, as well as the varnish previously used, and with the raw cashew nut oil. Strangely, no one reacted to the varnish, and only one to the cashew nut oil, so that some other factor was probably responsible for the outbreak.

Every detail in the handling of the varnish was investigated and studied. It was found that at the end of the working day the men would remove the varnish that adhered to the skin with solvasol.<sup>1</sup> The latter material is a violent chemical skin irritant, especially if allowed to stay in contact with the skin for any length of time. Questioning of the men revealed that they were accustomed to remove the varnish with a piece of cotton saturated with solvasol and then dry their hands without washing, thus leaving traces of the violent irritant in contact with the skin.

This outbreak of dermatitis was solved in the following manner:

1. Tongs were devised to handle the motor parts which were dipped into the varnish and hung up to dry.
2. The varnish adhering to the inside of these parts was removed with solvasol by the men wearing rubber gloves.\*
3. A non-irritating, harmless solvent† was found which readily removed any adhering varnish from the workers' arms and forearms. Soap and water easily removed this solvent from the skin.

Later, three samples of varnish were secured from the manufacturers.‡ One of the samples secured came from the Canadian branch of this firm. The other two were secured from the American branch.

\*Neoprene gloves, manufactured by "Surety Rubber Co.," Carrollton, Ohio.

†Oxyquinoline, diethylene glycol ethyl ether acetate in a petroleum distillate.

‡Irvington Varnish and Insulation Company.

## CASHEW NUT OIL DERMATITIS—LOCKEY

Forty-one men were tested with these samples. Nine of these were negroes. They had negative reactions to the patch tests. The remaining thirty-two men, with one exception, also were negative. The latter developed a dermatitis at the site of testing, with varnish manufactured by the American branch of the firm. None of the men reacted to the varnish manufactured by the Canadian branch of the firm.

All of the samples that were submitted had alkaline reactions. However, the pH of the Canadian varnish was around 8, whereas the pH of the so-called H.E. 107 manufactured by the American branch was around 7, and the pH of the regular American manufactured H. varnish 612 C. was around 5.

The man who developed dermatitis at the site of patch testing reacted to the varnish labeled Regular H. 612 C., having a pH of 5. Incidentally, this man is subject to severe attacks of ivy poison and poison oak. His family history is also positive for allergy.

A group of men were also tested with samples of American manufactured varnish, H.E. 107, which had been diluted with solvasol. All of the men reacted to these tests, indicating that the solvasol played an important part in the second outbreak of dermatitis.

The nine negroes were tested with varnish which had been diluted with solvasol. They had positive reactions, however, which were not as severe as those seen among the white men.

### CONCLUSIONS

1. The first outbreak of dermatitis described was definitely due to faulty treatment of the raw cashew nut oil present in the varnish. The reactions that the men exhibited were typically those found in individuals sensitive to the resinous oils of poison ivy, oak and sumac. Raw cashew nut oil is a known skin irritant.

2. The second outbreak of dermatitis was due to improper handling of the solvent "Solvasol," which is a chemical irritant to anyone if allowed to stay in contact with the skin long enough.

3. Individuals with an allergic background should not handle varnish that has a cashew nut oil base, especially those with a history of being sensitive to poison oak, ivy and sumac.

4. During the process of handling varnish and solvasol, the time of skin exposure was reduced several hundred per cent by the use of tongs and gloves. A non-irritating, harmless solvent was found with which to remove any varnish that may be present on hands and forearms of the men.

5. The pH of the varnish may be of some importance. However, there was no appreciable difference in the amount of skin irritation produced by various samples that were used in testing.

6. Some individuals mildly sensitive to raw cashew nut oil, who persist in handling it, say they eventually "become hardened to it." They apparently develop an immunity through exposure.

## CASHEW NUT OIL DERMATITIS—LOCKEY

7. Finally, by administering cashew nut oil extract intramuscularly the so-called "hardening process" can be accelerated and desensitization produced in sensitive individuals who work with cashew nut oil.

### CONCLUSIÓN

1. La primera erupción descrita de dermatitis fué definitivamente debida al imperfecto tratamiento del aceite del anacardo crudo, presente en el barniz. Las reacciones que los hombres presentaron fueron típicamente las encontradas en individuos sensibles a los aceites resinosos de hiedras venenosas, roble, zumaque. El aceite de anacardo es un conocido irritante de la piel.

2. La segunda erupción de dermatitis fué debida al uso impropio del disolvente "Solvasol" el cual es un producto químico irritante que positivamente irritará la piel de cualquiera, si se lo deja estar en contacto con ella por largo tiempo.

3. Individuos con antecedentes alérgicos y especialmente aquellos con historia de ser sensibles al roble, zumaque y hiedras venenosas no debían tocar ningún barniz que tenga por base aceite de anacardo.

4. Durante el procedimiento del uso del barniz y Solvasol, el tiempo de la exposición de la piel fué reducido varios cientos por ciento mediante el uso de pinzas y guantes. Se encontró un disolvente el cual no es ni irritante ni dañoso, para remover cualquier barniz que puede haber en las manos y antebrazos de los hombres.

5. El pH del barniz puede ser de alguna importancia. Sin embargo no hubo una notable diferencia en la cantidad de la irritación de la piel producida por varias pruebas que fueron usadas en el experimento.

6. Algunos individuos que siendo medianamente sensibles al aceite de anacardo y que persisten en el uso de éste, dicen que con el tiempo se vuelven insensibles a éste. Aparentemente desarrollan inmunidad exponiéndose.

7. Finalmente administrando extracto de aceite de anacardo por vía intramuscular, el llamado "hardening process" (proceso de desensibilización) puede ser acelerado y producir insensibilidad en individuos sensibles que trabajan con aceite de anacardo.

### REFERENCE

1. Wasserman, David, and Dawson, R. Charles: The synthesis of cis- and trans-3-(pentadecenyl-8')-veratole, a dihydro derivative of usushiol dimethyl ether. Department of Chemistry, Columbia University. Received October 12, 1942.

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Substitutes for Kapok are now being made from the floss of the cattail, a tall marsh plant (*Typha latifolia*) and from common milkweed plants (*Asclepias*), and are used in life belts, marine mattresses, cushions and for heat and sound insulation.

# Editorial

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## RENDER UNTO CAESAR

The announcement of the merger of the "Eastern" and "Western" Societies into the Academy of Allergy, the news of the growth of the American College of Allergy, the reports of the Committee to study "X" hay-fever, the recent meeting in St. Louis of the Association of Allergists for Mycological Investigation just prior to the Sixth Annual Forum on Allergy all raise the question in the minds of many as to which direction we are going with our organizations of allergists.

While most of us would like to see just one big society which can speak officially for us to organized medicine and to the public, there is much to recommend the independence of these several groups. Real progress tends to come through the operation of groups led by independent, dynamic personalities. Regimentation and dry rot tend to come with centralization.

## THE ANNUAL MEETINGS

As we see, the several organizations should, by and large, stick to the fields in which they find themselves today. The only function which the Annual Forum on Allergy has is to give to the newcomer a place to discuss clinical allergy and to offer to the physicians an extremely intensive and comprehensive instruction in the field of allergy and its progress. It should not attempt more.

For the time being at least, the College, in our opinion, should devote itself directly to the task of making better physicians out of all who practice in the field of allergy. Its programs, therefore, should be largely clinical programs, but much more detailed than those of the Forum. Its research reports should consist largely of the immediately practical. This means that they will have to do for the most part with a refinement of methods. In this connection, it is to be hoped that the committee on bio-assay will not go commercial, but will follow the plans originally suggested of preparing assayed material, in order to force the assay of all materials put on the market and withdrawing gradually from the field as such, assayed materials which go into production in the laboratories of commercial houses.

The function of the Academy should be, we feel, first the recognition of accomplishment, and, second, the stimulus of investigation into the fundamentals underlying the allergic reaction.

From time to time, groups will appear which are formed for coöperative research upon special subjects, such as we now have in the "X" hay-fever group and the group on Mycology. These, we feel, should be and should remain independent organizations, but they should expect and

## EDITORIAL

should receive the wholehearted support of both the College and the Academy. They should be given a chance to teach the physicians of North America that which they know for certain at the Annual Forum on Allergy; their clinical investigations should be given a hearing at the meeting of the College, and their basic research should find expression on the floor of the Academy. If these plans can be continued in a general way, allergy will progress very rapidly. There is no need for bickering and personalities. We are all concerned with learning more with which to help our patients.

## THE JOURNALS

So, too, with our publications. The *Journal of Immunology* ought to have all papers dealing with the basic immunological aspects of allergy; the *Journal of Allergy*, those papers reporting on the allergic reactions which are not so fundamental or which have a decidedly clinical slant; papers dealing with clinical allergy belong in the ANNALS OF ALLERGY. There is left the letters of The International Correspondence Club of Allergy, where one may express opinions, give advice, report little shortcuts in the technique of practice, and generally disport oneself as at the luncheon sessions of the national meetings—"informal, practical expressions of opinion!"

## BIBLIOGRAPHIC SERVICES

There is no need, in our opinion, for abstracts in any of the journals. Much valuable space is thereby wasted. This space should have been given over to the earlier publication of the original articles. The Staff of the Jewish Hospital of Brooklyn continues to give us good abstract service.

For nearly two years now, the Letters of the International Correspondence Club of Allergy have given a "spot" bibliography of the literature on allergy. The object has been to place on the subscriber's desk, within three weeks after its appearance, the reference to each and every item of interest to an allergist. At the same time, the mailing address of the author is given if it is in the United States or Canada. Otherwise, an attempt is made to have at the Club's headquarters a microfilm for lending purposes. These are designed primarily to aid the worker who wants to build and maintain his own complete library.

More recently the ANNALS OF ALLERGY has presented the same material from sixty to ninety days later, but has grouped it under titles, so that one with more restricted interests can use them more easily. This serves the useful purpose of helping the worker who wants to have all items of immediate interest called to his attention. Finally, of course, for older reference, we all depend upon the Index Medicus.

So, after all, there is not—or should not be—much overlapping or duplication in allergy on this continent. Mistakes may be made. Things may get out of place as they often do on a busy day. Allergy, however,



## EDITORIAL

is much better organized and implemented to do a good job than most fields of medicine.

Given a good supply of basic research, we, all working together, can prepare to bridge the gap of several years, which naturally exists between the results of research and their application by the family physician and reduces it to a matter of months. If we can continue to coöperate, there are great things ahead for the allergic patient. JONATHAN FORMAN.

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### THE SIXTH ANNUAL FORUM ON ALLERGY

The Sixth Annual Forum on Allergy was held January 22 and 23, 1944, at St. Louis, Missouri.

Despite restrictions in transportation and hotel facilities, it was the best attended and one of the most enthusiastic meetings ever held by The Forum since this international postgraduate society was founded in 1938 by Dr. Tell Nelson, Dr. Karl D. Figley, and Dr. Jonathan Forman.

The object of the organization as originally specified, is to provide in peacetimes a forum for the younger members and to offer an intensive postgraduate instruction on clinical allergy to physicians working in other fields.

The Forum's Gold Medal for outstanding contributions to Clinical Allergy was presented this year to Robert A. Cooke, M.D., of New York City. Many of Dr. Cooke's former students who have become illustrious in the field of allergy were present to pay tribute to the teacher who has been foremost in advancing the knowledge and standards of Allergy and whose influence has been felt by all physicians interested in this branch of medicine.

Dr. Cooke's accomplishments in Allergy, as pointed out by Dr. Harry Huber when presenting the medal, are too numerous to enumerate here, but they are well known as milestones in the progress of Allergy. It is the earnest wish of all that Dr. Cooke may continue these valuable contributions for many years to come. F.W.W.

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### THE CHICAGO MEETING

The program of the first annual convention of the College, June 10 and 11, at Chicago, will be held on the fourth floor of the Palmer House in the same rooms which will be occupied by the AMA sessions subsequently. The fourth floor is on the same level as the scientific exhibits for the AMA. An excellent entertainment is being arranged for the Saturday evening informal banquet. Barring unforeseen exigencies of the war, this meeting should be one of the largest convocations of allergists ever held in America.

The speakers' list contains some of the foremost distinguished allergists in the country. The College, now an established international allergy society with a membership embracing a majority of the notable allergists representing all groups, will always be known for its leadership in accomplishing a democratic unity when furthering investigative and clinical allergy.

—F. W. W.



# Progress in Allergy

Under the direction of ETHAN ALLAN BROWN

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## **An Index of the Proprietary Drugs and Mixtures Commercially Available for the Symptomatic and Adjuvant Treatment of Bronchial Asthma**

**ETHAN ALLAN BROWN, M.R.C.S. (London), L.R.C.P. (England), F.A.C.A.†**  
Boston, Massachusetts

**F**OR the treatment of bronchial asthma, there are advertised to physicians and patients, more than two hundred commercial products. Those which are not simple drugs are, of course, not Council Accepted. Nevertheless, by direct and indirect advertising, these commercial mixtures are made known to many thousands of patients who purchase them in enormous quantities often at exorbitant prices.

In this phase of their business, the more ethical drug houses are, occasionally, as reprehensible in their conduct as is the quack vendor of a nostrum. Skillful advertising casts an aura over simple drugs sold under copyright trade names which confound the ignorant patient, making him pay a premium for its supposedly special virtues. When financial considerations are important, the best possible medication should be prescribed at the lowest possible cost, especially when the cost, as in public clinics, represents taxation and contributions borne by the entire community.

The following list will then serve several useful purposes. Given the name of the commercially available preparation, its composition is noted so that a true evaluation of it may be made. Given a patient who has used one of the listed products, its composition known, his relief from a placebo type of nostrum or lack of it from an accepted combination of drugs helps measure the severity of the symptoms, telling us how amenable they may be to symptomatic or psychological relief.

Physicians who prescribe their own preparations or are instrumental in the purchase of drugs for public clinics or hospitals can quickly discover what may be purchased at the lowest possible unit cost.

The list is compiled from a number of sources, among others, by word of mouth from patients, from advertising literature, the catalogues of the large drug houses, the columns of the *Journal of the American Medical Association* and *Hygieia* all checked, when listed, by the *Modern Drug Encyclopedia*.<sup>1</sup>

The inclusion of any product in this list is not to be taken either as a recommendation for its use or an animadversion upon its maker. The products, many in type, and wide in variety, were chosen for listing because the literature advertising them states that they could be, should be, or might be useful, often among other conditions, in the treatment of bronchial asthma. The author would appreciate having his attention

<sup>1</sup>The incidental expenses for this work were defrayed in part by grant from The Asthma Research Foundation, Inc., Boston, Massachusetts.

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## PROGRESS IN ALLERGY

drawn to any proprietary remedy or nostrum which has inadvertently been omitted so that at some future date, if indicated, an even more complete list may be published.

*Acidogen*: (Abbott) Urea nitrate (0.194 Gm.). The disintegration of the substance within the body yields urea and free acid, temporarily decreasing the blood alkaline reserve.

Bottles: 60 capsules, 1-2 daily with meals.

*Adalin*: (Winthrop) Bromo-diethyl-acetyl-carbamide: Carbromal (0.324 Gm.) A sedative and hypnotic which it is said does not affect the heart, blood pressure, or respiration.

Bottles: 25 tablets, one or more three times daily.

*Adrenal Medullary Products*: These are known as Epinephrine, Adrenalin, Adrin, Epinine, Supranephrin, Suprarenalin, Suprarenin, and others. Excepting for the fact that some are natural and some synthetic, all present with slight differences the properties of Epinephrine.

*Adrenal Medullary Pills*: (Schieffelin) The adrenal residue, each pill listed as being equivalent to Epinephrine 4 m. The adrenal residue liquid, also available, contains 4 Mg. of Epinephrine per c.c.

*Adrenalin*: (Parke, Davis) Epinephrine (*See below*).

*Adrin*: (Sharp & Dohme) Epinephrine (*See below*).

*Afenil*: (Bilhuber-Knoll) and (Merck): Calcium Chloride Urea—10 per cent Aqueous solution in 10 c.c. ampoules. An organic calcium solution for intravenous administration for the correction of blood calcium deficiency.

Single ampoules: for intravenous administration, 1-2 daily.

*Alergene*: (Johnston, Holloway) Emulsion and capsules (3 m.) containing a combination of concentrated linoleic and linolenic acid unsaturates with wheat germ oil.

Emulsion: 32 oz. 1-3 tablespoonfuls daily.

Bottles: 100 capsules, 1-3 daily.

*Amazine*: (Lipoidal) A solution of proteolytic enzymes.

Vials: 30 c.c.

Ampoules: 1 c.c. (12), 8-16 m. every other day, intramuscularly.

*Amrodine*: (C. D. Searle & Co. Each tablet contains:

Aminophyllin	0.097 Gm.
Racephedrine hydrochloride	0.024 Gm.
Phenobarbital	0.008 Gm.

Bottles: 100; 1000 tablets. 1-2 tablets three times daily.

*Amonidrin*: (Breon)

Ammonium Chloride	0.194 Gm.
Ephedrine Hydrochloride	0.008 Gm.
Potassium Guaiaccol Sulphonate	0.194 Gm.
Calcium Creosotate	0.016 Gm.
Benzocaine	0.002 Gm.
Oleoresin Cubebs	0.0018 Gm.

Bottles: 100 tablets, 1-4 daily.

*Amyl Nitrite*: (Burroughs-Wellcome), (Lilly), (Parke, Davis). (Sharp & Dohme)

Ampoules: 3 m. and 5 m. By inhalation for temporary relief, when necessary.

*Antrocol*: (Poythress)

Atropine Sulphate	0.32 Mg.
Phenobarbital	0.0162 Gm.
Colloid of Sulphur	0.02 Gm.

Bottles: 100 tablets, 3-4 daily.

*Apocactin*: (Merrell) A combination of vegetable extracts in tablet form.

Fluidextract Crataegus	0.1540 c.c.
Fluidextract Cactus	0.0308 c.c.
Fluidextract Apocynum	0.0123 c.c.
Fluidextract Collinsonia	0.1232 c.c.
Fluidextract Avena Sativa	0.2464 c.c.

The extract is similar in composition, and contains, in addition, alcohol 53 per cent.

Bottles: 100 tablets, 4 daily.

Bottles: Extract 1 oz. 10 drops in water every 3-4 hours.

*Arleaps*: (Arlington) Capsules 5 Gr.

Acetylsalicylic Acid	0.130 Gm.
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# PROGRESS IN ALLERGY

- Phenobarbital 0.026 Gm.  
 Ephedrine Hydrochloride 0.026 Gm.  
 Alkaline Base q.s.
- Bottles: 25 and 500 capsules, 1 night and morning. Available in capsules, gr. 3, for children.
- Aspidospermine, Conine and Lobeline Compound:* (Chicago Pharmacal Co.) Tablets containing the three substances listed.  
 Bottles: 100, 500 and 1,000 tablets, 2 tablets in hot water, every 15 minutes to 2 hours.
- Asthma-Sera:* (R.M.B. Laboratories, Seattle, Washington) Described in JAMA as a brown liquid, having the odor of sarsaparilla and containing a laxative drug and, in addition to the teaspoonful:  
 Strontium Iodide 0.3825 Gm.  
 Sodium Iodide 0.022 Gm.
- Bottles: 1-4 teaspoonfuls daily.
- Asthma-tabs:* (Asthma-Tab Laboratories, Kansas City, Missouri). Described in JAMA.  
 Potassium Iodide 0.356 Gm.  
 Fowler's Solution (liquor potassii arsenitis) 0.616 m.
- Tablets: three times daily.
- Asthmolysin:* (Beisner) A solution said to contain the active principles of the posterior pituitary and suprarenal glands.  
 Ampoules: 1 c.c.  
 Boxes of 10, 1-3 c.c. subcutaneously or intramuscularly.
- Aurol-Sulphide:* (Hille) A colorless solution of gold sulphide, containing 5 Mg. of combined salts per c.c., gold 87 per cent and sulphur 13 per cent.  
 Bottles: 1, 4 and 12 oz., 2-5 c.c., intravenously or intramuscularly, twice weekly, orally, 20 drops three times daily.
- Az-ma-syde:* (Asthma Remedy and Manufacturing Co.) Described in JAMA as being a dark brown liquid, having an odor of thymol, wintergreen and phenol, and containing cocaine hydrochloride 0.291 Gm. to 30 c.c. For use in especially prepared atomizer.
- Belephedral Compound:* (Chemico Laboratories) Each capsule contains:  
 Belladonna (powdered) 0.006 Gm.  
 Phenobarbital 0.02 Gm.  
 Stromonium (powder) 0.065 Gm.  
 Ephedrine Sulphate 0.016 Gm.
- Dose: 1 capsule, 3-4 times daily.
- Belladenal:* (Sandoz Chemical Works, Inc.) Tablets containing a mixture of the natural levorotatory alkaloids of belladonna, 0.00025 Gm. with phenobarbital 0.05 Gm.  
 Available also as suppositories.  
 Tubes: 20 tablets.  
 Bottles: 100 and 500. Maximum dose, 6 tablets daily.  
 Boxes: 6 and 30 suppositories, 1-2 daily.
- Bellafoline:* (Sandoz Chemical Works, Inc.) Tablets containing the levorotatory alkaloids of fresh belladonna leaves as the malic acid salts (0.00025 Gm.). Available for oral, injection and suppository treatment.  
 Bottles: 20, 100 and 250 tablets, 1-2, three times daily.  
 Boxes: 6, 20, 1-c.c. ampoules, .05- 2-c.c. injected daily.  
 Bottles: 10, 100 c.c., 10-20 drops three times daily.
- Benzedrine Inhaler:* (Smith, Kline and French) Each inhaler contains:  
 Amphetamine 0.325 Gm.  
 Oil of Lavender 0.097 Gm.  
 Menthhol 0.032 Gm.
- Dose: Two inhalations through each nostril, not more often than once hourly.
- Benzyl Benzoate:* [(Merck), (Mallinckrodt), (Hinson), (Fritzsche)]. The benzyl alcoholic ester of benzoic acid. Available as a liquid in several quantities and strengths.  
 Dose: Oral, 0.3-0.5 m. The 20 per cent solution 1-2 teaspoonfuls may be repeated in 20 minutes.
- Benzyl Fumarate:* (Abbott) (*See Benzyl Benzoate*).
- Benzyl Succinate:* (Merck), (Hinson) (*See Benzyl Benzoate*).
- Bromcalate:* (Endo Products, Inc.) Formerly known as Dermol, each ampoule contains:  
 Calcium Gluconate 0.5 Gm.  
 Strontium Bromide 0.5 Gm.  
 Dextrose 1.0 Gm.

## PROGRESS IN ALLERGY

- Boxes: 6, 25, 100, 10 c.c. ampoules, 1 ampoule, intravenously daily for several days, then twice weekly.
- Bromural:** (Billhuber-Knoll), (Merck) Alpha-mono-brom-iso-valeryl carbamide. A quickly acting somnificient containing neither a bromide nor a barbiturate.
- Tubes: 10 tablets (0.324 Gm.) 1 tablet, several times daily.
- Burnham Soluble Iodine:** (Burnham Soluble Iodine Co., Inc.) A standardized solution of iodine, containing 1.1 Mg. total iodine per drop.
- Bottles: 2, 4 oz. 5-40 drops in water before meals. Intravenously 1:30 in sterile saline. Intragluteally, full strength.
- Calcreose:** (Maltbie) Calcium creosote U.S.P. XI. The chemical combination, by weight, of equal parts of creosote and hydrated calcium oxide. The tablets contain:
- |                   |           |
|-------------------|-----------|
| Calcreose         | 0.194 Gm. |
| Extract Euphorbia | 0.064 Gm. |
| Tincture Lobelia  | 0.18 c.c. |
- Bottles: 100, 500, 1,000 tablets. One hourly until relieved, thereafter, every 2-3 hours.
- Calcidin:** (Abbott) A compound containing 15 per cent iodine, combined with lime and starch. Available in tablets, (0.029 m., 0.06 and 0.329 m.), powder and troches, and in combination with anesthesin, (0.019 m.), with camphor (0.019 m.), hy-drastine hydrochloride, (0.0002 Gm.), and hysocamine sulphate (0.0003 Gm.).
- Bottles: 100, 1000, 5000 tablets. 0.04-0.32, 4-5 times daily.
- Calcilact:** (Abbott) An effervescent granulated combination of calcium lactate (25 per cent) and lactose (45 per cent).
- Bottles: 6, 14 oz. 1 cupful in water, three times daily, one hour before meals.
- Calcium Gluconate:** Available in many forms, strengths, quantities and combina-tions from almost all drug houses.
- Caldex:** (Endo Products, Inc.) A liquid, each 10 c.c. of which contains 56 Mg. of calcium, in a dextrose solution.
- Boxes: 6, 25, 100, 10 c.c. ampoules, for intramuscular injection, every other day.
- Calevate:** (Crookes) A sterile aqueous stable, non-irritating solution of calcium levulinate containing 50 per cent more calcium than calcium gluconate.
- Boxes: 6, 25, 100, 5 c.c., and 10 c.c., ampoules for intravenous or intramuscular injection.
- Calglucon:** (Sandoz) Normal calcium gluconate. Available as a powder, granules and as effervescent and chocolate tablets.
- Tins: 30, 150, 1000 tablets. 1-2 three times daily. Powder, 1 teaspoonful, three times daily.
- Calcium Lactate:** Available from many drug houses in tablets and pills (0.324 Gm.) in various quantities and combinations.
- Calcium Levulinate:** Available from many drug houses in ampoule form for intra-venous therapy.
- Camphella:** (Pitman-Moore) A liquid available with or without ephedrine, each fluid ounce containing:
- |                          |             |
|--------------------------|-------------|
| Cinchonine Sulphate      | 0.130 Gm.   |
| Fluid Extract Belladonna | 0.0616 c.c. |
| Camphor                  | 0.130 Gm.   |
| Ephedrine                | 0.130 Gm.   |
- Bottles: 1 pint and 1 gallon, 1-2 teaspoonfuls when necessary.
- Cole's Endocrine Compound No. 16:** (Cole Chemical Co., Inc.) Each capsule con-tains:
- |                           |           |
|---------------------------|-----------|
| Pituitary (Anterior Lobe) | 0.130 Gm. |
| Suprarenal                | 0.064 Gm. |
| Calcium Lactate           | 0.064 Gm. |
| Calcium Phosphate         | 0.064 Gm. |
- Boxes: 100 capsules, one, three times daily.
- Daldrin:** (Sharp & Dohme) Each fluidounce contains:
- |                          |            |
|--------------------------|------------|
| Codeine Phosphate        | 0.064 Gm.  |
| Propadrine Hydrochloride | 0.064 Gm.  |
| Tincture Aconite         | 0.246 c.c. |
| Fluidextract Ipecac      | 0.123 c.c. |
| Sodium Citrate           | 1.296 Gm.  |
| Chloroform               | 0.123 c.c. |
| Aromatic Base            | q.s.       |
| Alcohol                  | 5 per cent |
- Bottles: 1 pint and 1 gallon, 1 teaspoonful every 2-3 hours.

# PROGRESS IN ALLERGY

**Delbiase:** (Fougera & Co.) A liquid described as containing the halogen salts of magnesium, and said to be a "biological stimulant."

Boxes: 6 ampoules, 5 c.c. 1 ampoule every other day, intramuscularly.

**Dionin:** (Merck) Ethylmorphine hydrochloride. A sedative and antispasmodic intermediate in action between morphine and codeine.

Bottles: 15 gr.  $\frac{1}{8}$  and 1 oz. 15-30 Mg. by injection.

**Diaterpine:** (Schieffelin) Each dessertspoonful contains:

Ethylmorphine Hydrochloride	0.004 Gm.
Terpin Hydrate	0.130 Gm.

Bottles: 16 oz. and 1 gallon, 1 dessertspoonful 3-4 times daily.

**Dyspne-Inhal:** (Wallau) A 3.5 per cent solution of epinephrine for use in a special nebulizer.

Vials: 5 c.c. for inhalation.

Similar solutions are available from Parke, Davis, Associated Physicians, Burroughs-Wellcome, U. S. Standard, Rorer and Armour. Their names suggesting the derivation from epinephrine. They consist of solutions of epinephrine, varying from 1:30-1:100 for the inhalation treatment of bronchial asthma.

**Elixir Ephedrate:** (Hart Drug Corp.) Each teaspoonful (4 c.c.) contains ephedrine hydrochloride (0.008 Gm.) and phenobarbital (0.008 Gm.) in special elixir base.

Bottles: 1 pint; 1 gallon. 4 teaspoonfuls, repeated as required.

**E.M.E. Syrup:** (Abbott) A mixture combining the relaxing effect of the ephedrine, the expectorant action of ipecac and the sedative effect of ethylmorphine. Each ounce contains:

Ethylmorphine Hydrochloride	0.016 Gm.
Ephedrine Hydrochloride	0.032 Gm.
Fluidextract Ipecac	0.523 c.c.
Chloroform	0.064 Gm.

Thyme and Menthol in a suitable base

Bottles: 4, 16 oz. and 1 gallon, 1 teaspoonful 3-8 times daily.

**Endiphrin Inhalant:** (Harrower & Co.) A 1 per cent solution of synthetic epinephrine in saline with a .5 per cent chlorobutanol as preservative, for inhalation therapy.

Bottles: 8 c.c. for inhalation only.

**Endophrin Solution:** (Harrower & Co.) See Epinephrine.

**Entodon:** (Winthrop) Hexamethyl diaminoisopropanol diiodide, also known as propiodal.

Boxes: 10 ampoules, 2 c.c., 20 per cent solution, 1-2 c.c. daily subcutaneously, intramuscularly or intravenously.

**Ephcaben:** (Kretschmar, Inc.) Each tablet (0.3 Gm.) contains:

Ephedrine	0.024 Gm.
Calcium Lactate	0.048 Gm.
Benzyl Succinate	0.097 Gm.
Amidopyrine	0.097 Gm.
Theophylline	0.048 Gm.

Vials: 20 tablets, 1-2 tablets daily.

**Ephedrine:** Available in a variety of forms including capsules, tablets, elixirs, ampoules, syrups and solutions manufactured by many of the commercial drug houses. Its properties are too well known to require listing although some of the products containing ephedrine but known by trade names not suggestive of their composition will be found listed in their alphabetical order.

**Ephedrol:** (Eli Lilly) A sedative expectorant. Each fluidounce contains:

Ethylmorphine Hydrochloride	0.016 Gm.
Ephedrine Hydrochloride	3.888 Gm.
Potassium Guaiacol Sulphonate	0.518 Gm.
Syrup Squill	1.848 Gm.
Alcohol	3 per cent
Syrup Tolu, Balsam and Menthol	

Bottles: 1 pint and 1 gallon, 1-2 teaspoonsful every three hours.

**Ephenaria:** (Drug Products Co., Inc.) Each fluid ounce contains:

Fluidextract Ephedra	3.696 c.c.
Fluidextract Sanguinaria	2.464 c.c.
Syrup of Squill	2.464 c.c.
Syrup of Tolu	1.232 c.c.
Syrup Ipecac	1.478 c.c.
Calcium Guaiacol Sulphonate	0.516 Gm.
Mentholated Aromatics	

Bottles: 1 pint and 1 gallon, 1-2 teaspoonfuls when necessary.

## PROGRESS IN ALLERGY

- Ephetal*: (Abbott) Each tablet contains:  
 Ephedrine Hydrochloride 0.024 Gm.  
 Phenobarbital 0.016 Gm.  
 Bottles: 40, 100, 500, 1-2 tablets every 2-4 hours.
- Ephetonin*: (Merck) Synthetic racemic epedrine.  
 Bottles: 20 tablets (0.0489 Gm.) 1 tablet every 3-4 hours.
- Epinephrine Hydrochloride*: Available in a variety of forms and concentrations from twenty-five or more manufacturers. Synthetic products of closely corresponding structural formulae will be found listed alphabetically by their trade names.
- Epinephrine-Ephedrine*: (Breon) Each ampoule contains:  
 Epinephrine 1:2000  
 Ephedrine 3 per cent  
 Sodium Bisulphite (Stabilizer) 0.15 per cent  
 Boxes: 12, 25 ampoules (1 c.c.) 5-10 m. subcutaneously or intramuscularly.
- Epinephrine in Oil*: (Squibb) A suspension (2 Mg.) of powdered epinephrine crystals in 1 c.c. of peanut oil.  
 Boxes: 12, 25 ampoules, .75-1.5 c.c.
- Epinephrine and Pituitary*: (Endo) Each ampoule contains:  
 Epinephrine Hydrochloride 0.8 Mg.  
 Pituitary U.S.P. 2 I.U.  
 Boxes: 12, 100 ampoules (1 c.c.) intramuscularly when necessary.
- Epimine*: (Burroughs-Wellcome) a synthetic type of epinephrine, the 1:100 solution being equivalent to aqueous epinephrine 1:1000.  
 Boxes: 10 Hypoloids (1 c.c.) 5-15 m. hypodermally, 1 c.c. in 500 c.c. sterile saline, intravenously.
- Epiphedrine Compound*: (Rorer) Each ampoule (1 c.c.) contains:  
 Epinephrine 1:2000  
 Ephedrine Hydrochloride 0.024 Gm.  
 Chlorobutanol 0.5 per cent  
 Boxes: 12, 25, 100 ampoules  
 Vials: 20 c.c., 1 c.c. subcutaneously when necessary.
- Epragen*: (Eli Lilly) Each pulvule contains:  
 Acetophenetidin 0.227 Gm.  
 Amytal 0.05 Gm.  
 Ephedrine Hydrochloride 0.022 Gm.  
 Acetylsalicylic Acid 0.13 Gm.  
 Bottles: 40, 500, pulvules. 1 morning and night, 4 daily, if necessary.
- Eprinal*: (United Drug) A solution of epinephrine hydrochloride 1:100 with chlorobutanol 25 per cent in physiological saline solution, for use as inhalation therapy. Available also as 1:1000 for injection.  
 Bottles: 5 c.c. and 1 oz. for inhalation by nebulizer.
- Erythrol Tetranitrate*: (Merck), (Burroughs-Wellcome) Known also as Tetronitrol, Tetranitrin and Erythrityl Tetranitrate.  
 Tubes: 24 tablets (0.016 Gm.). The adult dosage being one-half to one grain every four to six hours.  
 Bottles: 50 tablets (0.032 Gm.) 1-2 tablets every 4-6 hours.  
 Also available in "Tabloids" 0.016, 0.032 and 0.065 Gm.
- Ethyl Iodide*: (Burnham Soluble Iodine Co.) A form of iodide especially purified for inhalation purposes.  
 Bottles: 1, 8, 16 oz. by inhalation, the initial dose being 1.5 c.c. and the average 3 c.c. with a maximum of 5 c.c., increased by 0.5 c.c. daily
- Euphorbia Compound Syrup*: (Sharp & Dohme) Each fluidounce contains:  
 Tincture Euphorbia 7.776 c.c.  
 Syrup Squills 11.664 c.c.  
 Wine Ipecac 1.944 c.c.  
 Jamaica Dogwood 1.00 c.c.  
 Menthol 0.008 Gm.  
 Chloroform 0.130 c.c.  
 Syrup of Tolu q.s.  
 Bottles: 1 pint and 1 gallon, 1-2 teaspoonfuls when necessary. The adult dose being 1-2 teaspoonfuls repeated if necessary in two hours.
- Eupnine*: (Wallau) 1 c.c. contains:  
 Iodine 0.070 Gm.  
 Potassium 0.028 Gm.  
 Extract of Licorice 0.035 c.c.  
 Glycerin 0.070 c.c.  
 Infusion of Coffee 0.797 c.c.  
 Bottles: 100 c.c., 1-3 teaspoonfuls in water, daily.

## PROGRESS IN ALLERGY

**Felsol:** (American Felsol Co.) Each gram of powder contains:

Antipyrine	0.8694 Gm.
Iodopyrine	0.03 Gm.
Citrated Caffeine	0.10 Gm.
Lobeline	0.0001 Gm.

**Florence Formula:** (Florence Product Co.) Described by the JAMA as consisting of gray white tablets, each contains:

Potassium Iodide	0.179 Gm.
Fowler's Solution	0.0616 c.c.

1 tablet, three times daily.

**Franol:** (Alba Pharmaceutical Co.) Each tablet contains:

Dephedin (Benzylephedrine Hydrochloride)	0.021 Gm.
Phenobarbital	0.008 Gm.
Theophylline	0.130 Gm.

Bottles: 25, 100 tablets, 1-2 three times daily.

**Freebreath:** (O. W. Dean Co.) Described by the JAMA as consisting of a clear colorless fluid containing the odor of menthol, each teaspoonful containing:

Potassium Iodide	0.162 Gm.
Fowler's Solution	0.185 c.c.

1 teaspoonful when necessary.

**Frontier Asthma Remedy:** (Frontier Asthma Co.) Described by the JAMA as a brown odorless fluid. Each teaspoonful contains:

Potassium Iodide	0.3955 Gm.
Caffeine	0.049 Gm.
Arsenous Oxide	0.00108 Gm.

1 teaspoonful when necessary.

**Glandular Compound No. 10:** (G. W. Carnrick) Each tablet contains:

Suprarenal	0.130 Gm.
Pituitary (whole)	0.032 Gm.
Thyroid	0.006 Gm.
Anterior Pituitary	0.097 Gm.

Bottles: 40 tablets, 1-2 tablets, three times daily.

**Glykeron:** (H. Smith Co.) A mixture, each teaspoonful of which contains:

Codeine Phosphate	0.008 Gm.
Hyoscyamus	0.064 Gm.
Ammonium Hypophosphite	0.193 Gm.
Balsam Tolu	0.016 Gm.
White Pine Bark	0.224 Gm.
In Glycerin	

Bottles: 4, 16 oz. 1-2 teaspoonfuls every 2-3 hours.

**Hair's Asthma Cure:** (Dr. B. W. Hair) Described by the JAMA as consisting of a brownish liquid containing potassium iodide, glycerin, alcohol and water.

**Hayes Asthma Cure:** (P. H. Hayes) Hayes Asthma Cure consists of six mixtures are described by the JAMA as having the following ingredients:

- (1) A liquid containing oil of turpentine and peppermint, the dose, 20-30 drops daily.
- (2) A liquid containing potassium iodide, the dose, 15 drops three times daily.
- (3) A syrup containing potassium iodide, the dose, 30 drops at bedtime.
- (4) A liquid containing 1 per cent Iron Peptonate, the dose, 15 drops three times daily.
- (5) Capsules containing quinine sulphate (0.10 Gm.), the dose, 1 capsule daily.
- (6) Pills containing resin of jalop, the dose, 1 pill daily.

**Himalya:** Reported by *Hygeia* as consisting of a licorice and peppermint flavored solution of potassium iodide in alcohol and water.

**Hyodin:** (R. W. Gardner) A liquid containing, in each 100 c.c., 0.15 Gm. Hydrogen Iodide.

Bottles: 4, 8 oz., 13 teaspoonfuls in water, 30 minutes before meals.

**Hyomei:** A nostrum for inhalation therapy of Bronchial Asthma. Described by the JAMA as having the following composition:

Oil of Eucalyptus	80 per cent
Alcohol	10 per cent
Liquid Paraffin	10 per cent
Creosote (a trace)	



## PROGRESS IN ALLERGY

- Injectable De Heckel:** (Anglo French Drug Co.)
- |                                  |                |
|----------------------------------|----------------|
| Suprarenal Extract (total gland) | 0.03 per cent  |
| Saccharose                       | 2.00 per cent  |
| Redistilled Water                | 97.97 per cent |
- Boxes: 12 ampoules (2 c.c.) 2 c.c.-5 c.c. injected subcutaneously.
- Iodalos:** (George W. Wallau) A solution of iodine and peptone, of which 20 drops contain the equivalent of 1.0 Gr. of alkaline iodide.
- Bottles: 50 c.c., 20-50 drops in water or other liquids, daily, at meals.
- Iodival:** (Bilhuber-Knoll) Alpha-monoiodi isovalerylcarbamide (47 per cent Iodine)
- Tubes: 10 tablets (0.324 Gm.). One tablet three times daily.
- Iodotine:** (Eimer and Amend) A standard glycerole of Hydrogen and Iodide, each teaspoonful containing 0.064 Gr. of iodine.
- Bottles: 10 oz., 1-2 teaspoonfuls, 3-4 times daily before meals.
- Lane's Asthma Treatment:** (D. J. Lane) A nostrum described by the JAMA as consisting of a brown liquid, having an aromatic odor and containing:
- |                     |           |
|---------------------|-----------|
| Calcium Iodide      | 0.162 Gm. |
| Alcohol 11 per cent |           |
| Gentian (flavoring) |           |
- Leaven's Asthma Prescription:** (Leavengood Drug Co.) Described by the JAMA as consisting of a syrupy liquid, each teaspoonful containing:
- |                                       |            |
|---------------------------------------|------------|
| Potassium Iodide                      | 0.518 Gm.  |
| Sugar Syrup                           | 3.697 c.c. |
| Sassafras and Wintergreen (flavoring) |            |
- Dose: 1 teaspoonful, three times daily
- Lipiodine:** (Ciba) The ethylester of di-iodobrossidic acid, containing 41 per cent inorganically bound Iodine.
- Bottles: 30, 100 tablets (0.39 m.) 1-6 tablets daily.
- Cartons: 5 ampoules (1.5 c.c.) 1 ampoule, intramuscularly 1-3 times daily.
- Lobiadrin:** (Breon) Each tablet contains:
- |                               |           |
|-------------------------------|-----------|
| Powdered Extract Lobelia      | 0.016 Gm. |
| Calciumiodobenzenate          | 0.097 Gm. |
| Ephedrine Hydrochloride       | 0.016 Gm. |
| Powdered Extract Sarsaparilla | 0.008 Gm. |
- Bottles: 100, 500, 1,000 caplets, 1-2 every four hours and at bedtime.
- Loingia:** (Columbus Pharmacal Co.) A mixture containing lobelia, stillingia, ephedrine (0.016) and the oils of cajuput, lavender and cinnamon in syrup.
- Bottles: 1 pint, 20-30 m. when necessary.
- Luasmin:** (Brewer & Co.) Each capsule or timed enteric coated tablet contains:
- |                             |           |
|-----------------------------|-----------|
| Ephedrine Hydrochloride     | 0.032 Gm. |
| Phenobarbital               | 0.032 Gm. |
| Theophylline Sodium Acetate | 0.194 Gm. |
- The tablets differ from the capsules in having an enteric coating which dissolves four to five hours after ingestion.
- Bottles: 30, 100, 1 capsule and 1 tablet on arising and retiring.
- Lumodrin:** (Winthrop) Each tablet contains:
- |                         |           |
|-------------------------|-----------|
| Luminal (Phenobarbital) | 0.016 Gm. |
| Ephedrine Hydrochloride | 0.024 Gm. |
| Pyramidon               | 0.130 Gm. |
- Tubes: 10
- Bottles: 25. 1-2 tablets, 3-4 times daily.
- Naiodine:** "Logeais" An aqueous solution of stabilized sodium iodide 1 per cent.
- Boxes: 6 ampoules, 5, 10 and 20 c.c. for intramuscular injection 20-40 c.c. 2-3 times daily.
- Nazoid:** (Columbus Pharmacal Co.) Contains colloidal calcium gelatinate in appropriate aqueous solution.
- Bottles: Dropper, ½ ounce, cartons of 12. 3-4 drops in each nostril, 3 times daily.
- Nebulin A:** (Fred. Stearns & Co.) Contains epinephrine hydrochloride 1 per cent, alcohol 5 per cent, chlorobutanol 0.05 per cent with glycerin 7.5 per cent in an aqueous vehicle.
- Dropper Bottles: 7.5 c.c. applied with Nebulator as spray.
- Neo-Calcin:** (Rorer) A solution of calcium lebulinate 10 per cent.
- Boxes: 6, 12, 25, 100 ampoules (5 c.c. and 10 c.c.) for intravenous or intramuscular injection.
- Neo-Calglucon:** (Sandoz) A solution of the double salt calcium glucogalactoglycone equal to 10 per cent supersaturated solution of calcium gluconate.



## PROGRESS IN ALLERGY

- Boxes: 3, 10, 50 ampoules (5 c.c. of 10 per cent and 20 per cent solution) 5-10 c.c. for intravenous or intramuscular injection.
- Neo-Riodine "Astier":** (Gallia) An aqueous 10 per cent solution of the organic sodium salt of iodine, containing 0.1 Gm. of iodo-propanol sulphanate of sodium (iodine 40 Mg.) in each 1 c.c.
- Boxes: 10, 50 ampoules (5 c.c.). 1-5 c.c. for intravenous or intramuscular injection 3-4 times weekly.
- Neo-Symphefrin:** (Stearns) A synthetic vasoconstricting agent for topical application. Available in capsules, emulsion, jelly, elixir, and solution form in a number of strengths and mixtures.
- Nethacetin:** (Merrell & Co.) Each tablet contains:
- |                               |           |
|-------------------------------|-----------|
| Netho-ethyl-amino             |           |
| Phenyl propanol hydrochloride | 0.043 Gm. |
| Phenacetin                    | 0.226 Gm. |
| Acetylsalicylic Acid          | 0.30 Gm.  |
- Bottles: 100 tablets. As directed by the physician.
- Nethacol:** (Wm. S. Merrell Co.) Each fluidounce contains:
- |  |            |
|--|------------|
| Methylethylamino-phenylpropanol (Nethamine brand) hydrochloride                            | 0.065 Gm.  |
| Chloroform   | 0.061 c.c. |
| Fluidextract ipecac  | 0.061 c.c. |
| Ammonium chloride  | 0.648 Gm.  |
| Methol   | 8 mg.      |
| with n-butyl p-hydroxy benzoate (1:5000) and benzoic acid (0.1 per cent) as preservatives. |            |
- Bottles: 1 pint; 1 gallon. 1-2 teaspoonfuls, repeated as required.
- Neuroesine:** (Dios Chemical Co.) Each fluidounce contains:
- |                         |            |
|-------------------------|------------|
| Potassium Bromide       | 1.944 Gm.  |
| Ammonium Bromide        | 1.944 Gm.  |
| Sodium Bromide          | 1.944 Gm.  |
| Zinc Bromide            | 0.039 Gm.  |
| Extract Hops            | 0.039 Mm.  |
| Extract Belladonna      |            |
| Extract Hyoscyamum      |            |
| Extract Cascara Sagrada |            |
| Sugar                   | 4.431 Gm.  |
| Alcohol                 | 4 per cent |
| Glycerin                | 8 per cent |
- Bottles: 2, 4, 8 oz. 1 dessertspoonful in water, three times daily after meals.
- Novalene:** (Professional Laboratories) Each tablet contains:
- |                    |           |
|--------------------|-----------|
| Ephedrine Sulphate | 0.025 Gm. |
| Phenobarbital      | 0.016 Gm. |
| Potassium Iodide   | 0.162 Gm. |
| Calcium Lactate    | 0.162 Gm. |
- Boxes: 25, 100 tablets. 1 tablet, three times daily before meals.
- Padrophyll:** (Sharp & Dohme) Each tablet contains:
- |                          |           |
|--------------------------|-----------|
| Propadrine Hydrochloride | 0.032 Gm. |
| Theophylline             | 0.129 Gm. |
- Bottles: 100, 1000 tablets. 1 tablet every 4-6 hours.
- Pancreatin and Bile Salts:** (Smith-Dorsey) Known also as *Pancholate*. Each capsule contains:
- |                              |           |
|------------------------------|-----------|
| Pancreatin (triple strength) | 0.266 Gm. |
| Bile Salts                   | 0.097 Gm. |
- Bottles: 100, 500, 1000 capsules. 2 capsules before each meal.
- Panteric Tablets and Capsules:** (Parke, Davis) Each contains pancreatin, U.S.P. (0.324 Gm.).
- Bottles: 100, 500 capsules or tablets. 1-2 three times daily one hour after meals.
- Peptalmine:** (Wallau) A combination of the peptones of meat and fish, egg and milk.
- Vials: 50 tablets.
- Bottles: granules (165 Gm.). 2 tablets or 2 teaspoonfuls one hour before meals.
- Peptone Solution:** (Armour), (National Drug) A mixture of primary and secondary proteoses and peptones prepared from lean muscle for non-specific protein therapy.
- Boxes: 12, 50, 100 ampoules 5 per cent, 1-2 c.c. for intramuscular injection .5-Sc.c. Also available in 30 c.c. vials.

# PROGRESS IN ALLERGY

*Phospho-Nefrin*: (Schieffelin & Co.) The phosphate of levomethylaminoethanolcatechol.

Each 100 c.c. of the 1:1,000 solution contains:

Epinephrine (USP) as the phosphate	0.1 Gm.
Chlorbutanol	0.5 Gm.
Sodium bisulfite	0.1 Gm.
Sodium chloride	0.85 Gm.
Distilled water	q.s.

Bottles: 1 ounce (1:1000) Inject 0.2-0.5 c.c. of 1:1000 solution. For inhalation,

1:100 (Bottles 5 c.c., with dropper).

*Phyllophed*: (United Drug Co.) Each capsule contains:

Ephedrine Sulphate	0.032 Gm.
Phenobarbital Sodium	0.032 Gm.
Theophylline Sodium Acetate	0.194 Gm.

Bottles: 100 capsules, 1 when necessary.

*Pit-Ren*: (Drug Products Co.) Each capsule contains a combination of desiccated hypophysis, cerebri, epinephrine hydrochloride with tribasic calcium phosphate.

Packages: 100 capsules, 1-2 every three or four hours.

Packages: 12, 25, 100 hyposols (1 c.c.) for subcutaneous or intramuscular injection.

*Pituitary Extract and Epinephrine*: (National Drug) Each ampoule (1 c.c.) contains:

Liquor Pituitary	0.5 c.c.
Epinephrine U.S.P. 1:1000	0.5 c.c.

Boxes: 1 ampoule-vial (10 c.c.) 1-2 c.c. intramuscularly every 12-48 hours.

*Platt's Rinex Prescription*: (Clinical Laboratories) The capsules are described by the JAMA as containing:

Acetylsalicylic Acid	0.130 Gm.
Acetphenetidin	0.065 Gm.
Quinine	0.011 Gm.

The tablet contains:

Sodium Bicarbonate	0.220 Gm.
Sugar	0.0715 Gm.

*Potachlori-zem*: (Zemmer, Inc.) Each tablet contains in effervescent form:

Potassium Chloride	0.324 Gm.
Potassium Citrate	0.040 Gm.

Bottles: 100, 500 tablets, 1 tablet dissolved in water 3-4 times daily.

Bottles: Elixir 1 pint, 1 teaspoonful in water 3-4 times daily.

*Potassium Gluconate*: (Fred. Stearns & Co.) Each tablet (0.5 Gm.) contains approximately 80 mg. of available potassium and is equivalent to (0.162 Gm.) of potassium chloride.

Bottles: 100 tablets. 2 after meals.

*Pressyl*: (Anglo-French) Each ampoule contains:

Camphramine	0.194 Gm.
Pressedrine	0.048 Gm.

This mixture is said to combine the effects of camphor, epinephrine and ephedrine.

Boxes: 36 tablets (half above doses) 2-5 daily before meals.

Boxes: 6 ampoules, 1-2 subcutaneously or ½ ampoule intravenously.

*Propadrine Hydrochloride*: (Sharp & Dohme) Phenyl-propanol-amine hydrochloride. A synthetic broncho dilator similar in chemical structure and action to ephedrine and epinephrine. Available in solution, capsules, elixir and jelly forms in a variety of mixtures, quantities and doses.

*Proteolac*: (Searle) A solution of peptones and proteoses derived from defatted milk. Boxes: 6, 25, 100 ampoules 2, 5 and 10 c.c. for intramuscular injection 1-10 c.c. every 2-5 days.

*Prudine*: (Buffington) Each fluidounce contains:

Iodized Calcium	0.130 Gm.
Potassium Citrate	3.888 Gm.
Sodium Phosphate	0.016 Gm.
Dailybarbituric Acid	0.048 Gm.
Syrup of Wild Cherry and Tolu	

Bottles: 12 oz. and 1 gallon, 1 teaspoonful every 3-4 hours.

*Pseudo Ephedrine Hydrochloride*: (Burroughs-Wellcome)

Bottles: 25, 100, 500 tablets (0.032 and 0.064 Gm.) 1 tablet when necessary.

*Quictone*: (Continental) a tablet said to contain benzyl fumarate, ammonium succinate yohimbine (5 Mg.) and excipients.

Boxes: 25 tablets (0.5 Gm.) 1 tablet three times daily, 30 minutes after meals.

## PROGRESS IN ALLERGY

**Quineph:** "Leprince" (Wallau) This mixture is also known as Freinospasmyl.

Each tablet contains:

Quinine Hydrobromide	0.06 Gm.
Ephedrine Hydrochloride	0.02 Gm.
Phenyl-Methyl-Malonyl-Urea	0.03 Gm.
Powdered Belladonna Leaves	0.01 Gm.

Bottles: 40 tablets, 2-4 tablets daily when necessary.

**Racephedrine Hydrochloride:** (Upjohn) A racemic mixture of equal parts of dextro and levo ephedrine hydrochloride.

Bottles: 40, 250 capsules (0.024 Gm.) 1 capsule 1-3 times daily. Also available as a 1 per cent solution in a modified Ringers' solution for use as a nasal spray.

**Raz-mah:** (Templeton, Inc.) Described by the JAMA as consisting of capsules each of which contains:

Acetylsalicylic Acid	0.291 Gm.
Charcoal	0.065 Gm.
Caffeine	0.032 Gm.

**Respirin:** (Physicians Drug Co.) Each tablet contains:

Ephedrine Hydrochloride	0.008 Gm.
Caffeine	0.016 Gm.
Phenobarbital	0.016 Gm.
Extract Belladonna Leaves	2.16 Mg.
Antipyrine Salicylate	0.129 Gm.

Boxes: 50 tablets. 2 tablets every three hours.

**Riodine "Astier"** (Gallia) A solution of iodine (17 per cent in an iodized glyceric ether of ricinoleic acid).

Bottles: 50, 300 capsules (0.20 Gm.). 2-6 daily after meals.

**Riona Capsules:** (Sharp & Dohme) Each capsule contains:

Propadine Hydrochloride	0.048 Gm.
Acetophenetidin	0.129 Gm.
Acetylsalicylic Acid	0.194 Gm.

Boxes: 30, 100 capsules. 1 every three hours.

**Ryno:** (E. H. Ryno) Described by the JAMA as consisting of a solution of cocaine hydrochloride (99.95 per cent) for use in a special atomizer.

**Sajodin:** (Winthrop) Calcium Iodobehenate—a product containing iodine 24.5 per cent and calcium 4 per cent.

Bottles: 24 tablets (0.06 Gm.) 5-15 three times daily, one hour after meals.

Tubes: 20 tablets (0.51 Gm.) 1 daily.

Also available as powder.

**Sinufarm:** (Columbus Pharmacal Co.) A mixture containing iodoform, iodine, menthol, camphor and eucalyptol in vegetable oils.

Boxes: 12, 25, 100 ampoules (1 c.c.) for intramuscular injection 1 c.c. daily.

**Siomine:** (Pitman-Moore)

Bottles: 100, 500 capsules (0.0324, 0.065, 0.13 and 0.324 Gm.) As required.

**Sodium Salicylate and Sodium Iodide:** A mixture available from many manufacturers, the amount of each drug varying from 0.486-0.972 Gm. in addition to various amounts of guaiacol, creosote and other substances for intravenous injection.

**Spasmalgin:** (Hoffman LaRoche) Each tablet contains:

Papaverine Hydrochloride	0.021 Gm.
Pantopon	0.012 Gm.
Atrinal	0.001 Gm.

Tubes: 20 tablets

Bottles: 10 tablets. 1-2 tablets daily.

Cartons: 6 ampoules, 1-2 intramuscularly or subcutaneously when necessary.

**Stello's Asthma Cure:** (W. H. Muller) Described by the JAMA as being a liquid containing potassium iodide, cannabis, indica, glycerin and alcohol.

**Sufrogel:** (Heyden) A suspension of finely divided sulphur .3 per cent in gelatin.

Boxes: 3 ampoules (1 c.c. and 5 c.c.) intragluteally 0.2-0.4 c.c. every 8 days.

**Supraneprhin Solution:** (Rorer) A solution of epinephrine 1:100 for inhalation.

**Supraarenalin:** (Armour) Epinephrine.

**Supraarenin:** (Winthrop) Synthetic epinephrine.

## PROGRESS IN ALLERGY

- Tedral:** (Maltine) Each tablet contains:
- |                         |           |
|-------------------------|-----------|
| Ephedrine Hydrochloride | 0.024 Gm. |
| Phenobarbital           | 0.008 Gm. |
| Theophylline            | 0.130 Gm. |
- Boxes: 24, 120 tablets. 1-2 tablets when necessary.
- Theamin:** (Lilly) Theophylline (74.68 per cent), monoethanolamine (25.32 per cent). Available as powder, pulvules, encols and ampoules for oral, intramuscular and intravenous therapy.
- Thelo:** (Kenmore Pharmacy, Boston, Mass.) Each tablet contains:
- |                              |           |
|------------------------------|-----------|
| Ephedrine Sulphate           | 0.024 Gm. |
| Lobeline Sulphate            | 0.065 Gm. |
| Phenobarbital                | 0.008 Gm. |
| Theophylline Ethylenediamine | 0.130 Gm. |
- Bottles: 50 tablets, 1 when necessary.
- Theonitral Compound:** "Synergen" (Chemico) Each tablet contains:
- |                        |            |
|------------------------|------------|
| Theobromine Salicylate | 0.227 Gm.  |
| Calcium Salicylate     | 0.227 Gm.  |
| Sodium Nitrate         | 0.0216 Gm. |
| Phenobarbital          | 0.0216 Gm. |
- Bottles: 25, 50, 100 tablets. 1 tablet 2-3 times daily.
- Thiate Compound:** (Merrell) Each fluidounce contains
- |                               |           |
|-------------------------------|-----------|
| Potassium Guaiacol Sulphonate | 0.384 Gm. |
| Benzocaine Benzoate           | 0.016 Gm. |
| Sodium Monobenzy Succinate    | 0.324 Gm. |
| Sodium Salicylate             | 0.907 Gm. |
- Also available with codeine (0.064 Gm.).
- Bottles: 12 oz. and 1 gallon. 1-2 teaspoonsfuls when necessary.
- Torantil:** (Winthrop) An extract made from mucosa of the small intestines and desiccated kidneys of the hog. One unit inactivates 1 Mg. Histamine at 37.5° C. for 24 hours.
- Bottles: 50 enteric coated (5 units). 2-3 tablets three times before meals.
- Tribromauro:** (Chicago) An aqueous solution of neutral gold tribromide (0.003 Gm.). Bottles: 1, 5 pints, 1 gallon. 1-2 teaspoonsful 4-5 times daily.
- Tricalcine:** "Ferrier" (Wallau) A mixture containing calcium carbonate (3 parts), tribasic calcium orthophosphate (1 part), with magnesium oxide (2 per cent), and succrose. Available in powder, cachets, tablets, and injectable forms alone and combined with other drugs.
- Tucker's Asthma Specific:** (Dr. Nathan Tucker Asthma Specific Co.) Described by the JAMA as containing cocaine (0.234 Gm.) to the ounce, for use in a special atomizer.
- Vitamin F:** (Archer-Daniels), (Chicago), (Rorer). A mixture of unsaturated fatty acid, (linoleic, linolenic and isolenoleic). Available in doses varying from 1000-50,000 Sherman-Linn units, the usual dose being three perles of globules, three times daily after meals.
- Vonedrine with Ceepryn Solution:** (Wm. S. Merrell Co.) Vonedrine (brand of phenylpropylmethylamine) with Ceepryn (brand of cetylpyridinium chloride), aqueous isotonic solution, pH adjusted to 5.5. Bottles: 1-oz. dropper and pint. Used by dropper, spray, tamponade or displacement followed by suction.
- Webb's Prescription:** (Webb Chemical Co.) Each tablet as described by the JAMA contains:
- |                  |           |
|------------------|-----------|
| Potassium Iodide | 0.194 Gm. |
| Powdered Lobelia | 0.065 Gm. |
| Powdered Squill  | 0.065 Gm. |
| Sugar            | 0.032 Gm. |
- Dose: 1 tablet several times daily.

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**Annual Review of the Recent Literature on Hay Fever**

**HELEN C. HAYDEN, M.D., F.A.C.A.**

**Chicago, Illinois**

**I**N WORLD WAR I, little or no attention was paid to allergic conditions. The studies and researches carried on in the past twenty-five years have led to a recognition of the importance of allergic factors in the present war and adequate diagnostic facilities and care are for the most part now available to members of the armed forces. The necessity for classifying allergic patients, especially as to their ability to withstand the various conditions which arise in army life, is emphasized by Blank.<sup>3</sup> As a rule, only the major manifestations are picked up at the receiving centers; other evidences of allergy are recognized at the replacement and training centers. As French and Halpin<sup>14</sup> state, the incidence of allergy in the army closely parallels that in civilian life (i.e. 10 per cent) and "it is inevitable that many applicants will be rejected who should be retained and many will be inducted who should be discharged." It is estimated by Blank<sup>2</sup> that over 1 per cent of all the men entering the army will require allergic care. More than one-half of all the allergic cases fall in the respiratory group and approximately one-half of this group will be made up of seasonal hay fever. As would be expected, ragweed cases far exceeded those of grass, and there were only a few due to trees. French states that only 3 per cent of 1,269 patients from the 4th Service Command were classified as having hay fever of unknown origin, a type which is peculiar to this section of the country (Georgia).

Under the present military regulations, patients with mild hay fever are classified as 1A and are accepted for full duty; those with moderate symptoms as 1B are accepted for limited service, and those with severe hay fever or any form of bronchial asthma are disqualified. In many army clinics attempts are made not only to classify but to test and adequately treat every patient who reports with hay fever. Desensitization procedures are frequently continued where they have been given previously, and preseasonal, or coseasonal and palliative treatments are given as indicated. French and Halpin have demonstrated that adequate testing and desensitization can be done at a very low cost.

A report on allergic rhinitis and asthma in Hawaii is given by Young, Cook and Kawaski.<sup>35</sup> They believe that the climatic conditions and flora would be similar in many other tropical and semitropical areas in the Pacific. This report is timely and valuable because of the large numbers of our men stationed in these areas. Many members of the native and transient population suffer from allergic manifestations. The distinction between hay fever and allergic rhinitis is not well defined because of the perennial type of flora. If symptoms have appeared on the mainland, they are apt to be more frequent and severe in Hawaii. Symptoms due to exogenous factors are apt to be worse in hot dry weather while endogenous

## PROGRESS IN ALLERGY

symptoms are worse in the damp rainy season from November to March. Local dust is of prime importance, but there is a perennial yield of grass pollen, and algeroba or kiawe tree pollen and some monkey pod tree pollen. Sugar cane is not considered important. Desensitization with local dust, mixed grasses and algeroba pollen has been very effective in most instances.

Ailanthus (tree of heaven) pollen has been shown by Blumstein<sup>4</sup> to be the cause of hay fever and asthma in two patients whose symptoms occurred during the first three weeks in June, and specific desensitization was effective in relieving their symptoms.

Durham<sup>12</sup> suggests that *Kochia scoparia* pollen should be included in routine testing in the Mississippi Valley area, inasmuch as this member of the goosefoot family is spreading rapidly and is being found in sufficient amounts in the air to cause trouble.

A timely popular article by Sonnedecker<sup>29</sup> draws attention to the fact that hemp growing is being pushed by the government. This no doubt means that in time hemp may be an important cause of allergic symptoms.

A case of seasonal hay fever and asthma due to narcissus bulbs was reported by Derbes.<sup>10</sup> The patient, a farmer who worked with narcissus bulbs and had symptoms from June to December, reacted to an aqueous extract of the bulbs and received 50 per cent relief from desensitization with this extract.

The seasonal pollen incidence in England has been studied by Hyde and Williams,<sup>18</sup> who exposed slides daily. The pollen season extends from mid-February to late October and is due to tree, grass and later to herbaceous dicotyledons, but the latter produce little pollen and are of no importance.

Pollen sensitivity is a more frequent cause of nasal symptoms in southern California than foods, according to the report of Smith, Goodhill and Webb.<sup>28</sup> There are three districts, the coastal, intermontane and desert basin with varying flora depending upon meteorological conditions. Acacia, pepper, cypress and eucalyptus trees bloom year round as do Bermuda grass and many other plants, such as *Franserias* (ragweed), *Artemisia* (sagebrush), *Arteplex* (saltbrush), *Amaranth* and *Chenopods*.

Gottlieb and Urbach<sup>15</sup> have divided the United States into nine zones and have listed the plants which most commonly cause hay fever, the pollination times and the relative importance of each.

Detailed drawings and descriptions of atmospheric pollens are given by Wodehouse.<sup>34</sup> In this same publication Durham<sup>11</sup> has an excellent résumé on the allergenic molds which includes an historical review, methods of sampling and counting spores, tables of available information on spore counts and seasonal maps of the incidence of *Alternaria* and *Hormodendrum* for fifty-three cities in the United States.

From a study of exposed slides and plate cultures, Randolph and Squier<sup>23</sup> conclude that *Alternaria* spores are the chief cause of inhalant fungous allergy in Milwaukee and are present in relatively large numbers

## PROGRESS IN ALLERGY

from mid-July to mid-October, while *Hormodendrum* is considered of secondary importance.

By means of slides and plate cultures taken throughout the year Negroni and Fischer<sup>21</sup> have studied the atmospheric molds in Buenos Aires and have isolated 388 different types of fungi. *Penicillium* and *Cladosporium* were prevalent from July to October and *Aspergillus* and *Alternaria* from August to January. *Penicillium* was found most frequently, followed by *Cladosporium*, *Alternaria* and *Aspergillus*. Definite conclusions were not reached as to the curve of frequency of the different fungi in relation to the seasons of the year.

The Committee of Allergists<sup>9</sup> for the study of the unknown causes of hay fever and asthma report an improved technique for the collection, isolation and culture of air-borne mold species. The results of scratch tests with these extracts compare favorably with those obtained with other purified extracts (i.e. grass, ragweed and house dust).

No practical method for the direct volumetric census of air-borne allergens has yet been found. Frequent attempts have been made to convert the easily obtained gravity slide data to volumetric figures. In order to apply Stokes' law to the problem of volumetric air content, accurate data should be available on the specific gravity (density) of pollen granules. Durham<sup>13</sup> has found that the specific gravity of free-floating pollen grains contains little, if any, more moisture than commercially dried pollens. Approximate specific gravity figures are submitted for typical weed, grass and tree pollens.

A slowly absorbed pollen antigen has been sought for many years for use in very sensitive patients. Taub and Rubens<sup>32</sup> have prepared such a pollen in oil by electrically homogenizing lyophilized aqueous pollen extract into sterile sesame oil. This extract does not deteriorate at room temperature; it is more slowly absorbed, is less likely to produce severe reactions and permits higher dosages with a smaller number of injections.

Spain, Fuchs and Strauss<sup>30</sup> have improved their gelatin pollen extracts by combining aqueous pollen extract with gelatin which has been autoclaved for one and one-quarter hours at 20 pounds pressure. This solution does not require preheating, can easily be handled with a 26 gauge needle and because of its slow absorption rate has been especially useful in the treatment of very sensitive patients.

Colmes<sup>8</sup> has continued desensitization through the ragweed season with one group of patients and has discontinued all therapy after August 15 in another group. As judged by written reports kept by the patients during the season, both groups did equally well.

Sternberg<sup>31</sup> reports marked improvement in the condition of a patient suffering from autumnal somnolence after ragweed desensitization. During August and September for a period of eleven years, this patient was dull, listless, confused and totally incapacitated. Ragweed desensitization resulted in marked improvement.



## PROGRESS IN ALLERGY

In two excellent articles, Loveless<sup>19</sup> has demonstrated practical applications for the immunological studies on the thermostable antibody. In the one, fifty-two ragweed patients were observed during three to five pollinating seasons and the number of "intensity-hours" of hay fever for each was compared with the amount of thermostable antibody in his circulation during the season. A close parallel was found to exist between the amount of antibody and the clinical degree of insusceptibility. Seventy-nine per cent in one group and 19 per cent in another showed a close correlation in all years but one. The degree of clinical resistance associated with a given amount of thermostable antibody varied decidedly with the individual, some requiring much more antibody than others for effective immunity. Loveless suggests that pollen-sensitive patients should be treated according to their particular immunologic needs, rather than empirically as in the past. The immune state of each individual may be used as a guide to treatment, especially if this is determined periodically during the first year of successful treatment. The conjunctival reaction obtained with threshold amounts of antigen may serve as a simple index as to the patient's immunity.

In a second article, Loveless,<sup>20</sup> assuming that the thermostable antibody plays a protective role in hay fever, has studied methods of producing optimum amounts of it. Inasmuch as normal individuals react more quickly and strongly to a secondary or "booster dose" of pollen extract, it was thought that pollen-sensitive patients might experience an enhanced response to "booster" or secondary doses of pollen extract some months after their primary experience with it. By use of the modified Prausnitz-Küstner technique it was found that following their education with a primary series of subcutaneous injections of ragweed extract, pollen-sensitive patients regularly responded to secondary doses given after months of freedom from treatment with an enhanced or accelerated production of thermostable antibodies. The longer the period of rest, the lower the resting titre, and the faster the secondary stimulation, the greater was the immune response. In general, the response to the secondary stimulating doses was more favorable when a large initial dose had been given, but during the secondary stimulation the phenomenon of "immunological ceiling" was more frequently encountered. Those patients who had been given perennial treatment for hay fever showed no tendency to an enhanced response. These findings suggest that a patient will do better if he is intensively treated for several months during the first year with periodic tests for immunity to determine his responsiveness and the level of immunity at which he will be comfortable. The goal the second season can then be the amount of antibody that has previously been found effective.

In a preliminary report, Hampton, et al<sup>21</sup> have described a precipitin method for the determination of the thermostable antibody. A potent rabbit antiragweed serum was produced and the sera of ragweed-sensitive patients was taken before and after treatment. These sera were heated to



## PROGRESS IN ALLERGY

destroy the thermolabile (reaginic) antibodies and equal parts of ante-treatment heated serum and strong ragweed extract and post-treatment heated serum and strong ragweed extract were shaken and allowed to stand in the icebox over night. Each was then mixed with anti-ragweed rabbit serum and incubated at 37°C. More precipitation occurred in the mixture containing ragweed antigen, heated ante-treatment serum and anti-ragweed-rabbit serum than in the corresponding tests containing post-treatment serum. The antibodies in the post-treatment serum appeared to have neutralized the ragweed antigen, leaving less to react with the rabbit antiserum. The conclusion was that the precipitin method compared favorably with the passive transfer test for detecting the thermostable antibody and is much simpler to perform.

Simon,<sup>27</sup> in studying the relationship of ragweed to its close relatives, concludes that hypersensitivity of this type develops as a result of allergenic stimulation. The pollens of ragweed and their relatives, in addition to species-specific allergens, have multiple allergenic determinants which vary in their distribution. Persons exposed simultaneously to a group of allergens may become sensitive to certain members of the group, and not to others; while another person, exposed to the same group may become sensitized to different members of the group.

By means of peptic digestion of giant ragweed extract, Harsh and Huber<sup>17</sup> have shown a marked loss of activity, not accounted for by dialysis alone, with a small but constant amount of activity in this pollen which is unaffected by proteolytic digestion. They believe that the major part of the activity of giant ragweed pollen is due to a digestible protein, some substance inseparably associated with it, or some substance active only in the presence of the protein.

Sherman<sup>28</sup> tested ragweed patients with nucleic acids and other related compounds and found that only a small percentage of patients reacted and in no case was the reaction as large as to ragweed. The significance of the phenomenon was not clear.

Brown and Benotti<sup>6</sup> subjected ragweed extract to heat to determine the amount of nitrogen precipitated and found that a constant amount of nitrogen is precipitated by heat, the same amount being precipitated by other precipitating agents specific for albumin. The true albumin content is small.

Cohen and Friedman<sup>7</sup> studied the fractions of ragweed pollen which were precipitated by various concentrations of ammonium sulfate to see if the different portions of the ragweed antigen stimulated the formation of separate antibodies. If the reagin and the neutralizing antibody are separate entities it must also be assumed that their formation is stimulated by different chemical portions of ragweed antigen. A water-soluble and water-insoluble portion were obtained with each precipitation and these fractions were further separated by freezing and thawing into pigmented and unpigmented portions. In addition, a crystalline material was also

isolated from several of the portions. Skin tests showed that all these fractions retained their skin test activity except the crystals from the non-protein nitrogen fraction. All fractions except the non-protein nitrogen crystals neutralized a strong reagin-bearing serum. This indicated that either there was some common antigenic material in all fractions or that there were several reagents reacting specifically with different antigens. Cross-neutralization tests with three of these fractions demonstrated that each of them neutralized the skin test sites with itself but did not neutralize their activity to tests with the other two fractions. This indicates that there are at least two and possibly three separate reagents in the serum tested. Precipitin tests with rabbit anti-ragweed serum gave positive results with all fractions.

Brown and Benotti<sup>5</sup> believe that it is desirable in the state of present knowledge to define pollen solutions in terms of total nitrogen content per millimeter of the whole extract or by Coca's definition of the Noon pollen units. After maximal precipitation with phosphotungstic acid, there is still present in the supernatant fluid nitrogen-containing material which is undeniably active (as shown by endermal testing of the supernatant fluid).

Newell<sup>22</sup> has studied the fractions of low ragweed extract prepared with concentrated potassium phosphate, ethyl alcohol of varying strengths and aqueous extracts precipitated by ammonium sulfate at one-half and full saturation by means of electrophoresis. All fractions were active as shown by skin tests and the substance extracted in 60 per cent alcohol at  $-15^{\circ}\text{C}$ . and by 80 per cent alcohol were found to be the most nearly pure of all fractions. None of the chemical means of fractionation has yielded any fraction which is even approximately a pure chemical substance.

Timothy pollen extract, studied electrophoretically by Abramson et al<sup>1</sup> resembles ragweed extract in that there is a major, colorless, slow-moving component and six or more negatively charged pigmented fractions which migrate more rapidly. Both the colorless and pigmented components are biologically active. There was a greater amount of the colorless material than pigmented and there is a question as to the immunological specificity of the various fractions.

According to Rockwell,<sup>24</sup> the phosphotungstic acid precipitate of crude ragweed extract contains all of the active antigens and can be separated into a major and four other active antigens. These antigens are flavonal-carbohydrate peptide complexes. Fraction 1, the major antigen, is separated out immediately as the hydrochloride.

A more detailed study of Fraction 1 or the major antigen has been made in a later report by Rockwell.<sup>25</sup> From a determination of the percentage concentrations of nitrogen, sulfur, carbon, hydrogen and oxygen, he has calculated the number of atoms of each element and determined the formula and the molecular weight. The empirical formula is  $\text{C}_{205} \text{H}_{349} \text{O}_{70} \text{N}_{38} \text{S}$ , and the molecular weight 4,496.084. By chemical analysis, it is found to contain one molecule of a flavonal pigment (isorhamnatin), one

## PROGRESS IN ALLERGY

molecule of a pentose (arabinose), and two polypeptide molecules. The structural formula is depicted.

Weil and Reddin<sup>83</sup> believe that the immunological mechanisms found in human beings can also be demonstrated in cattle. They found, after injections of pollen extract into heifers, evidence of dermal supersensitivity in cattle to ragweed, have demonstrated the presence of reagins and neutralizing antibodies in the serum and have obtained similar neutralizing effects with the sera of rabbits injected with pollen extract.

## CONCLUSIONS

The war is increasing our knowledge of the occurrence of allergy in all parts of the world.

During the past year outstanding contributions have been made to the chemical and immunological studies of pollen extracts.

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## HYPERSENSITIVITY FROM INHALATION OF ATOMIZED FLUID ANTIGENS

Inhalations of finely atomized specific antiserum have been suggested for the prevention and treatment of influenza. A possible hazard of this experimental procedure has just been recorded by Hopps and Moulton.<sup>†</sup> Their report is based on tests made with five antigens (nonhomologous) on guinea pigs and rabbits. The animals were placed in a closed chamber and exposed for twenty minutes to finely atomized particles of the various serums. By the third of the three weekly exposures many mild reactions were observed. By the fifth week of such treatment allergic reactions were severe. Several of the sensitized animals died in the chamber during exposure to the atomized specific antigen. Since serious allergic reactions and fatal anaphylactic shock have occurred in animals from a procedure which has been suggested for human beings, further human studies should be pursued with great caution. Routine use of aerosols of this nature is not now desirable.—*JAMA*, December 11, 1943.

<sup>†</sup>Hopps, H. C., and Moulton, Stanley: Active Hypersensitivity from Inhalation of Finely Atomized Fluid Antigens, *Soc. Exper. Biol. & Med.*, (to be published).

## PROGRESS IN ALLERGY

### Annual Critical Survey of the Recent Literature on Bronchial Asthma

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**A** SURVEY of the recent literature on bronchial asthma has yielded no sensational results. During that period no one has made any remarkable contributions in this field. There have appeared, however, numerous articles, both in the United States and abroad, the most important of which deal with the military aspects and with treatment.

#### MILITARY ASPECTS

The official ruling of the United States Army is that no one with an allergic condition of "significant" degree shall be admitted to the army. A similar ruling, perhaps enforced more strictly, is used by the United States Navy. Despite these orders, however, large numbers of allergic individuals have found their way into the armed services and among these many have already been returned to civil life.

The problem existed in World War I and has continued to the present time. The following letter from Rear Admiral Ross T. McIntire, Surgeon General, United States Navy, dated November 23, 1942, is self-explanatory:

"This will acknowledge your letter of October 26, 1942, regarding data for your proposed book on Bronchial Asthma.

"This Bureau has no information on the percentage of allergic individuals in the Navy or Marine Corps. However the following data are available on admissions to the sick list and discharges from the service:

Diagnosis	Admissions		Discharge from service	
	1940	1941	1940	1941
Allergy, otherwise unclassified	12	26	0	8
Asthma	62	156	50	123
Hay Fever	11	17	4	14
Urticaria	149	253	2	6

"The average strength of the Navy and Marine Corps in 1940 and 1941 was 202,614 and 348,926, respectively.

"Most of the larger Naval hospitals have medical officers specially qualified as allergists."

A study of the table reveals that the percentages quoted as regards allergy in the Navy and Marine Corps is approximately 0.11 per cent in 1940 and 0.12 per cent in 1941. This compares with the figure of 0.5 per cent in World War I. The reduced percentage probably indicates that the Medical Officers of this era more fully realize the hazards of admitting allergic individuals, especially those who were asthmatic, into the armed services.

## PROGRESS IN ALLERGY

Some interesting articles have recently appeared. French and Halpin<sup>17</sup> have reported on army allergy as seen in the Fourth Service Command, with headquarters at Atlanta, Georgia. They established an allergy section in the Fourth Corps Area and organized allergy clinics at each station hospital staffing these with medical officers, to many of whom they gave brief but intensive courses in allergy. They manufactured, at very low cost, standardized extracts for skin testing and for treatment and distributed these extracts to each clinic, together with a routine procedure for treatment. In twenty-one clinics in this area, 3,419 military and 498 civilian allergic individuals were cared for. The number of clinics was more recently increased to fifty-nine.

Of the asthmatic patients, 283 had asthma due only to inhalation of pollen (109 from ragweed, 34 from grass, 140 from both grass and ragweed). All gave positive skin tests for the respective pollens and, "as a whole, preseasonal and coseasonal therapy produced very satisfactory relief." An additional 192 individuals suffered from pollen hay fever and pollen asthma. Besides these two groups there were 759 patients who had perennial asthma; of these 187 were also sensitive to pollens; house dust seemed to be the chief exciting factor in perennial asthma.

The severe cases of hay fever (sixty-five) were hospitalized but 71 per cent of the 1,153 allergic patients requiring hospital care were asthmatic; they numbered 820 and received the usual epinephrin and ephedrin for symptomatic relief. There were successful attempts to make certain wards "allergen-free." An average of 18.1 hospital days per patient was recorded for 1,153 hospitalized allergic patients. Bronchial asthma was the foremost cause for prolonged stay in the hospital. Much of this delay was due to the waiting period before certificates of disability discharge arrived. Of the 3,917 patients seen in the allergy clinics only 195 (4.3 per cent) were discharged from the service and 184 of these were asthmatics, chiefly men who had perennial asthma. By contrast, 267 allergic patients (6.3 per cent) were successfully treated, reclassified and retained in military service.

Blank<sup>4</sup> reports that from June 1, 1941, to October 1, 1942, he saw 1,833 cases at the allergy clinic at Fort Eustis, Virginia. This figure represented 1.5 per cent of the personnel. Fifty per cent of these cases were due to allergic involvement of the respiratory tract (hay fever, asthma, perennial rhinitis, allergic sinusitis and nasal polyps). The remainder consisted of dermatologic, ophthalmologic and gastro-intestinal allergies and migraine. Disability discharges were given to seventy-eight patients, seventy-six because of asthma. Blank outlines the treatment given patients at his post and advocates the establishment of allergy sections at all training centers and general hospitals.

In a paper dealing chiefly with the socio-economic status of selectees in the Boston district, Hyde and Kingsley<sup>20</sup> note that 495 (about 0.8 per cent) of 60,000 registrants were rejected because of one or more disqualifying allergic conditions. Of these 355 suffered from bronchial



## PROGRESS IN ALLERGY

asthma. The authors note that the percentage of rejection is definitely highest (1.4 per cent) in the semi-rural one-family areas and lowest in the crowded tenement districts (0.6 per cent). This finding confirms the general impression that hay fever, in particular, and bronchial asthma are more common in rural districts, probably because of increased exposure to pollen and animal feathers and danders.

From Hawaii comes a report which is of special interest to many in our armed forces. Young, Cook and Kawasaki<sup>67</sup> studied 114 patients who suffered from exogenous asthma, fifty-one with endogenous asthma, and fifty-seven with allergic rhinitis—these were seen at the allergy clinic of the Tripler General Hospital at Honolulu for twelve consecutive months. Because the climate is semi-tropical, pollen is perennially present, and therefore causes perennial rhinitis and asthma; the resulting symptoms are more prolonged and more severe in Hawaii than in the United States. The symptoms of endogenous asthma are more severe in damp or rainy weather, while those of exogenous asthma are more severe when the weather is hot and dry. Many cases of asthma, especially of the endogenous type, occur in Hawaii in persons who had no pre-existing symptoms in the United States, and such individuals usually give a negative family history for allergy. Local dusts which contain pollen of native grasses, weeds and trees are the most common exciting inhalant allergens. Ragweed is either absent or unimportant, but pollen from the algeroba tree is very important and abundant from March to September. Desensitization with extracts of local dust and pollen of grass and algeroba is beneficial in the treatment of exogenous asthma and rhinitis.

### ETIOLOGY OF ASTHMA

Davidson's<sup>11</sup> contention that house dust does not contain a specific allergen but is merely a mixture (cotton, flax, jute, wool, silk, animal hairs and feathers, glue, kapok, orris root, pyrethrum, tobacco) has again aroused considerable argument. Most men disagree with his view and believe that a specific allergen is present, probably a decomposition product of various substances, especially cotton and kapok. Davidson made cutaneous and intracutaneous tests on 100 patients who showed definite skin reactions to house dust; he found that each of these patients gave positive skin tests to one or more of the twenty or more ingredients of house dust mentioned above.

Argument followed the reading of a paper by Browning<sup>8</sup> on mold extracts. He found that 37 per cent of a series of thirty-eight mold extracts were irritants and of no clinical value. Of the remaining twenty-four extracts only three had a diagnostic efficiency as high as 70 per cent; these extracts averaged about 60 per cent efficiency, a figure considered as only mediocre. In the discussion Prince agreed that his mold extracts were not too accurate but pointed out that (1) in a high percentage of patients with confusing mold tests passive transfer tests were usually negative, and (2) when mold tests occur among botanical groups passive

## PROGRESS IN ALLERGY

transfer is frequently positive. By selecting molds for therapy that most consistently show definite positive reactions on scratch testing, weaker titrations and passive transfer Prince's mold therapy has become more encouraging.

Feinberg, in a series of 600 allergic patients, used scratch tests almost exclusively, either with concentrated extracts or with the dry powder. In a group of 253 patients who were clinically allergic to molds positive skin tests for molds were obtained in 241 (96 per cent); in another 351 patients clinically not sensitive to molds, only ten were definitely positive (3 per cent). Harris agreed with Feinberg concluding that their extracts are not irritating. Almost all patients with a good clinical history of allergy to alternaria mold gave positive intracutaneous tests to this mold and also developed symptoms when powdered alternaria was blown into the nostrils.

Gelfand<sup>21</sup> has added tragacanth to the list of vegetable gums which can cause rhinitis and asthma; other allergenic gums are karaya gum, which causes symptoms chiefly through the use of hair-waving lotions, and acacia (gum arabic) widely used in the printing trade in off-set sprays. In a study of gum sensitivity among workers in a gum factory Gelfand stated (a) gum sensitization is an occupational risk for predisposed persons; (b) a period of time (usually about a year) is required after first exposure before acute symptoms occur; (c) tragacanth can cause severe symptoms; (d) hyposensitization with allergenic gums is difficult, if not impossible; (e) some workers who become sensitized may afterward spontaneously develop tolerance [such tolerance is very unusual in sensitivity to inhalant allergens]. He also showed that tragacanth can neutralize all the reagins to gum arabic but arabic only partially neutralizes the reagins to tragacanth. These two differ in genus and species but are members of the same family (Leguminosae), while karaya belongs to a different family (Sterculiaceae).

Thomas<sup>59</sup> and Saunders<sup>54</sup> report respiratory allergy to arsphenamines in two physicians. Thomas' patient gave a personal history of asthma, angioneurotic edema, migraine and allergic dermatitis. Inhalation of powdered neo-arsphenamine caused asthma; the doctor attempted to desensitize himself by ingestion of 3 mg. of neo-arsphenamine dissolved in 1.8 c.c. of fluid but severe asthma followed within twenty minutes. A patch test was positive.

Saunders, a syphilologist who had been continually exposed to arsenicals for eight years but had a negative family and personal history for allergy, has for the last three years had sneezing, rhinorrhea and asthma after opening ampules of mapharsen, arsphenamine or neo-arsphenamine. Inhalation of tryparsmide had no effect. Patch tests were negative but a scratch test with a 6 per cent solution of neo-arsphenamine was strongly positive; both kinds of tests were followed by constitutional reactions.

These two cases add to the small number previously reported. The reviewer has had a similar case, also a syphilologist, who, despite a negative



## PROGRESS IN ALLERGY

personal and family history for allergy, developed rhinitis and asthma when opening ampules of neo-arsphenamine. Symptoms also came on some years after first exposure. A skin test (scratch) was strongly positive. In an attempt at hyposensitization intradermal dilution tests were carried out and were strongly positive for the 1:1,000,000 dilution. Asthma quickly followed and the patient refused further treatment. Passive transfer was negative.

Mirvish<sup>39</sup> of South Africa finds that in children foods are more often responsible for asthmatic attacks than inhalation. In this country we seem to be tending to the opposite opinion. Yogi<sup>66</sup> notes that the incidence of bronchial asthma in Formosa is much higher than in Japan proper. The incidence was high during the humid months (October-May) and low during the dry summer months (June-September). Molds are probably important in the humid months. And Derbes and Engelhardt<sup>14</sup> in a statistical study of the Charity Hospital in New Orleans found that although bronchial asthma is common among negroes the admission rate was only about 65 per cent that of white asthmatic patients.

From the *psycho-allergic* point of view Rogerson<sup>52</sup> finds that the asthmatic child has a special personality type with above the average intelligence. He is apt to be irritable, aggressive, quick to respond, over-anxious, insecure and lacks self-confidence. Leavitt<sup>32,33</sup> reports only six cases of bronchial asthma in 9,500 patients with dementia praecox in four institutions (Kankakee, Manteno, Elgin and Jacksonville). This gives a percentage of 0.06 per cent in marked contrast to the higher percentage (1 to 4 per cent) in the general population of the United States. Leavitt also found only ten cases (0.08 per cent) of bronchial asthma in 11,647 psychotic patients in Kankakee, Manteno, Elgin and Jacksonville. These patients were diagnosed as presenting dementia praecox, manic depressive, paranoia and paranoid conditions. The mental condition of these patients had no relationship to bronchial asthma or vice versa. All of the ten patients with bronchial asthma gave a positive family history. There were no asthmatic patients among those who were mentally defective or had epilepsy (Dixon State Hospital).

One statement of Leavitt should be condemned. He says that bronchial asthma is a neurotic condition: "a neurosis which is manifested by such a clear-cut clinical entity as bronchial asthma." The old idea that neurosis is the cause of asthma should have been discarded years ago.

In an effort to explain the well-known observation that allergic manifestations are frequently worse just before or during menstruation Hans-Pruss and Raymond<sup>25</sup> tested the strength of reagins of four young women who were ragweed-sensitive. By passive transfer tests on five young males with blood taken at six different periods of the menstrual cycle they found that the size of the resultant wheals was greatest on the last day of menstruation. They, therefore, concluded that the highest reagin titer is on this last day.

Thomas<sup>60</sup> reports a case of seasonal asthma in a dog with symptoms

## PROGRESS IN ALLERGY

limited to the ragweed season. This confirms Wittich's observation of hay fever in a dog, also due to ragweed (*J. Allergy*, 12:247, 1941).

Brown and Goitein<sup>6</sup> attempt to classify the etiology of bronchial asthma into various levels: (1) ontogenic, (2) phylogenic, (3) biogenic, (4) humorogenic, (5) cytogenic, (6) somatogenic, (7) neurogenic and (8) psychogenic. Under each classification the factors are listed in detail.

### PATHOLOGY

Hilding<sup>26</sup> has made an excellent contribution. He analyzed the records and pathological material from thirty-nine fatal cases of asthma, twelve cases of influenza and ten cases of bronchopneumonia. The lining of the bronchi was markedly changed. Goblet-like cells had replaced the normal columnar ciliated cells. The ciliary mechanism was apparently absent, and a viscid, mucinous secretion blocked the air passages and was adherent to the walls. The gradual occlusion of the air passages eventually caused asphyxiation and death. Hilding believes that removal of secretions from the lower respiratory tract is largely dependent on ciliary action and stresses the importance of the loss of this ciliary function with occlusion and sometimes with death. He urges mechanical removal of viscid secretions by aspiration through a bronchoscope or even by tracheotomy in desperate cases. Hilding's observations and advice are very logical.

Schiller, Colmes and Davis<sup>55</sup> found that cor pulmonale due to chronic bronchial asthma is more common than generally recognized. In a study of sixty-nine patients with bronchial asthma, with autopsy findings in fifteen cases, they report that abnormalities of the heart are common. Electrocardiograms showed right ventricular strain and myocardial damage in a large number: 13 per cent right axis deviation, 9 per cent tendency to right axis deviation, and this deviation was present in 18 per cent of patients with a history of asthma for more than ten years. Of twelve patients who died after asthma of six or more years, five died in congestive failure; predominant hypertrophy of the right ventricle was found in four of these. [One might remark that all of their fatalities occurred in patients who were forty-six or older, mostly over sixty; their incidence of decompensation seems much too high. There is no reference to eosinophilia in the blood, sputum nor in the tissues, and emphysema itself occurred in only two cases. The diagnosis of allergic bronchial asthma in all these cases seems not to have been proven.]

The clinical and autopsy findings of eighty-two adults and four children with "fatal asthma" are reported by Lamson, Butt and Stickler.<sup>31</sup> A wide variety of conditions were found to simulate the clinical symptoms of asthma. These included marked interstitial emphysema, extensive atelectasis, pulmonary fibrosis, bronchiectasis, chronic rheumatic heart disease, hypertension and syphilitic aortitis. The authors rightly warn against the use of morphine in bronchial asthma since many patients in this series died shortly after its use. They correctly found that bronchial asthma rarely, if ever, causes conspicuous abnormalities of the heart and circulation.

## PROGRESS IN ALLERGY

This paper, with its large number of patients and its varied pathological conditions, grouped together under the heading of "fatal asthma" evidently deals with all sorts of abnormalities within the chest. As Unger said in discussing the report, "We could solve all these arguments if we would use the term 'bronchial asthma' to mean allergic asthma. The word 'asthma' unless qualified, should not be used in all the other conditions which he describes, including rheumatic heart disease and pulmonary tuberculosis."

Vance and Strassmann<sup>63</sup> performed autopsies on seven persons who died after injections of foreign proteins. Two of the patients were asthmatic, the other five presumably non-asthmatic. An asthmatic child died shortly after an intracutaneous test with a mixture of extracts of silkworm, wool and kapok. [Death has previously occurred after intracutaneous skin tests, a strong argument in favor of preliminary scratch tests.] One asthmatic adult died after an injection of ragweed extract used in treatment. The other five died following antitoxin injections made with horse serum. The marked inflation of the lungs and other signs of asphyxia were thought due to bronchospasm. Eosinophile cells were abundant in the bronchial walls and there was a striking resemblance of the lungs of both the asthmatic and the non-asthmatic patients.

### SYMPTOMATOLOGY

The frequent co-existence of vasomotor or allergic rhinitis with bronchial asthma is well known. Urbach and Gottlieb<sup>64</sup> found vasomotor rhinitis present in 38 per cent of 379 cases of asthma; the two conditions appeared at about the same time in about one-half of these cases. When nasal symptoms began within two years preceding or following the onset of asthma the same allergen was usually responsible. When longer intervals occurred the two conditions were usually brought on by different allergens.

Sprague<sup>56</sup> reports co-existence of bronchial asthma and pulmonary tuberculosis in eight cases during the past ten years, with seven of these discovered in the past five years. All were picked up by x-ray films and in three cases tuberculosis was not previously suspected. This incidence seems a bit high. Positive sputa were not obtained.

In a metabolic study, Donovan and Harsh<sup>15</sup> found that asthmatic children ingested slightly more sodium when on high sodium or high potassium diets than did non-allergic children. The asthmatic children also excreted more sodium and more acid in the urine. There was little difference in the two groups in the concentration in the plasma of potassium and sodium.

Osgood and his co-workers<sup>44,45</sup> have studied blood pressure fluctuations in respiratory obstruction, including asthma. They gradually obstructed breathing in cats at the trachea and in healthy medical students at the mouth. Similar results were found: (a) the greater the obstruction the greater the fluctuation of the blood pressure during respiration; and (b) whatever the degree of respiratory obstruction the highest blood pressure

## PROGRESS IN ALLERGY

occurs during expiration, the lowest during inspiration. They then showed this to be true in the obstruction which occurs in bronchial asthma. Between attacks of asthma systolic blood pressure taken during expiration is usually about 3 mm. Hg. higher than during inspiration. But during attacks this difference increases according to the severity of the seizure and may reach 50 mg. or even more in extremely bad spells. When the asthma subsides the fluctuations return to normal. This change is so constant as to be a useful clinical sign, indicating approximately the degree of respiratory obstruction.

Osgood and Ehret<sup>46</sup> then checked these findings after subcutaneous injections of epinephrin and intravenous administration of 0.24 or 0.48 gram of aminophyllin. They found that if adrenalin gives relief the respiratory systolic blood pressure fluctuations decrease to or near the normal. Aminophyllin, however, even if relief is obtained, causes decrease in fluctuations but not so markedly as with epinephrin. If no relief is obtained with either drug the fluctuations remain wide. The authors suggest that the principal action of aminophyllin in relieving asthma is by increasing the blood flow through the pulmonary circulation by vasodilation and that its bronchodilating effect is of secondary importance.

## DIAGNOSIS

Children who cough longer than six weeks and without evidence of whooping cough or other disease should be investigated from the allergic point of view, says Marks.<sup>36</sup> Respiratory foci of infection should be treated at the same time. If both methods of treatment fail change of climate should be tried. Gittins<sup>22</sup> classifies laryngotracheobronchitis in children into four types: (1) infectious, (2) traumatic, (3) allergic, either angioneurotic edema or asthma, and (4) spasmodic (croup). The allergic group is usually associated with a positive familial or personal history of allergy and with wheezing and prolonged expiration. Tracheotomies are rarely necessary in the allergic type.

Friedberg<sup>18</sup> points out once more that asthmatoïd breathing can occur from a variety of clinical conditions which narrow the caliber of the tracheobronchial lumen. This pathologic narrowing in addition to the physiologic shortening and contraction of the bronchi is probably responsible for the expiratory wheezing. Bronchoscopy is very important in making a correct diagnosis and in removing the cause of the obstruction. Friedberg urges bronchoscopy in all atypical cases of bronchial asthma. He gives eight interesting case reports with cure in five of the patients following removal of foreign bodies.

Browning<sup>9</sup> writes on the differentiation of bronchial asthma from sighing dyspnea and from cardiac asthma. This last condition is best diagnosed by determining the circulation time by the lung to tongue time test, according to the author. [This test is probably not necessary inasmuch as cardiac asthma is characterized by the presence of a cardiac condition—coronary occlusion, syphilitic aortic regurgitation, hypertension or chronic

## PROGRESS IN ALLERGY

nephritis, and especially by the finding of moisture at the base of the lungs.] Reeves<sup>50</sup> reminds us of the importance of fungus infections in pulmonary disease. He advises iodides but states that in monilia and blastomycosis infections the iodides should be preceded by desensitization.

Gutmann<sup>24</sup> found that in ten allergic individuals, of whom nine had asthma, there was an increase of pressure in the central artery of the retina, as shown by his new ophthalmodynamometer. [Study of his cases, however, shows that six of these patients had a blood pressure of 150 or over, and only one had a normal blood pressure.] Brown and Goitein<sup>7</sup> blindfolded individuals and asked them to draw pictures of themselves. Fifty asthmatics drew sketches which the authors placed in their Group B (repetoid). The significance of this work remains to be seen.

The Weltman reaction has again been discussed. Furstenberg and Scherlis<sup>20</sup> made 298 tests in a group of fifty-eight patients with allergic conditions. They conclude that the routine use of the test is of little clinical value. Dees<sup>72</sup> studied the reaction in 224 asthmatic patients and believes that the test is of aid in detecting the presence of infection and fibrosis in asthmatics.

## TREATMENT

A large number of articles deal with the treatment of bronchial asthma. They are chiefly concerned with various non-specific measures which add refinements to our previous knowledge.

Boyer<sup>5</sup> has a very good critical article on the value of aminophyllin and of related xanthine derivatives. He confirms the effectiveness of aminophyllin in the treatment of bronchial asthma especially in patients who have become epinephrin-fast. He states that it is less effective than epinephrin and should not supplant the latter. As regards the use of aminophyllin and similar xanthine derivatives in cardiac asthma, angina pectoris and coronary occlusion, Boyer finds little support for its continued use although the drug does increase the output of urine and probably does increase the strength of the myocardial contraction.

Merrill<sup>38</sup> has recently reported three cases in which death quickly followed the intravenous use of aminophyllin. One patient had an acute coronary occlusion; the second had bronchial asthma associated with a high blood pressure (200/90) and with heart sounds of poor quality; the third had a cor bovinum with acute cardiac decompensation. The author rightly concludes that the intravenous use of aminophyllin in acute cardiac conditions, e.g., cardiac asthma, is dangerous. He is probably incorrect when he suggests that the drug may cause death in bronchial asthma. When 0.24 or 0.48 gram of aminophyllin is slowly injected intravenously in bronchial asthma prompt relief is usually obtained and no harm results. Transient nausea and vomiting may occur if the solution is injected too rapidly. Its use in bronchial asthma should be continued, but morphine is a much safer and much more effective drug in acute cardiac disease.

Dees<sup>13</sup> is very enthusiastic about the use of rectal suppositories con-

taining 0.25 gm. aminophyllin. By inserting these twice daily she has been able to reduce symptoms in patients with severe asthma, even in status asthmaticus. Relief occurred quickly in most cases, within twenty minutes, and lasted from four to twenty-four hours. The method is well worth a trial.

Three recent papers deal with efforts to prolong the action of epinephrin. Richards<sup>51</sup> used rats in his experiments and found that the toxicity resulting from intramuscular injections of epinephrin in oil is about equal to that of a freshly prepared aqueous solution of the drug. Ordinary commercial solutions which contain sodium bisulfite are much more toxic. Toxic symptoms and deaths with oil suspensions are usually but not always delayed as compared with results with aqueous solutions. Richards also found that when the particles of epinephrin in oil are ground to a smaller size the resultant suspension is less toxic, less potent and less stable.

Naterman<sup>43</sup> believes that delayed absorption of epinephrin in oil is due to the insolubility of the adrenalin base in tissue fluids rather than to the oil. He has, therefore, added sodium thioglycolate to prevent oxidation and injects his new suspension subcutaneously. There was no loss in potency in fifteen months. Suspensions may contain 2 to 4 mg. of base per c.c. The usual dose is 1 to 4 mg. He states that no epinephrin side-effects occur even when three or more times the usual quantity of epinephrin is injected; the period of relief is longer and the local reaction is less. He, therefore, claims that his suspension is superior to the ordinary oily preparations. Abramson<sup>1</sup> prepares epinephrin in gelatin by adding sufficient urea to the gelatin solution to maintain the gel in the sol state at room temperature. This does away with the use of autoclaving and the necessity of heating prior to injection.

Nethamine hydrochloride, an ephedrin-like drug, was given to twenty-three asthmatic patients, with improvement in eleven. Friedman and Cohen<sup>19</sup> also report improvement in fourteen of twenty-three patients with hay fever and also claim relief in a few patients in whom the use of ephedrin had failed. The toxic effects are less than those of ephedrin and in the ordinary therapeutic dose there were no significant changes in the blood pressure or pulse rate. This drug has been used in the Allergy Clinic at Northwestern University Medical School but the results were very doubtful. Another drug has also been extolled. The good results claimed have, however, not been corroborated. Melton<sup>37</sup> was able to relieve sixteen of nineteen attacks of asthma by the intravenous use of 50 to 100 mg. of nicotinic acid. Lesser relief came from the oral administration of 50 to 100 mg. three times daily over a protracted period. I have tried this procedure both orally and intravenously in four asthmatic patients but no relief occurred. And yet another broadside at the claims for histaminase (Torantil) comes from Peshkin and his co-workers.<sup>47</sup> They found that the oral administration of 50 units daily for from two to twenty weeks,



## PROGRESS IN ALLERGY

averaging nine weeks per patient, was of no benefit in forty-eight allergic children, of whom twenty-eight suffered from asthma.

Sedatives are frequently necessary in the treatment of bronchial asthma. Maietta<sup>35</sup> injects intramuscularly 2 c.c. doses of a mixture of equal parts of ether and peanut oil. Although there is a temporary burning pain no induration abscess results. The injection may be repeated in several hours as indicated. The patient becomes quieter in a few hours and is relieved. This mixture is especially indicated, says Maietta, in epinephrin-fast patients.

Demerol, a new analgesic, has been helpful in bronchial asthma as well as in other conditions where sedation is necessary. Batterman and Himmselbach<sup>8</sup> have shown that demerol possesses three chief actions: analgesia, spasmolysis and sedation. Its use is, in many ways, equal or superior to that of morphine, and, as regards asthma, it does not endanger life since it does not lessen expectoration. The authors state that an acute attack of asthma can be relieved within ten minutes by the subcutaneous injection of 35 mg., a dose far below that required to produce analgesia or sedation. The bronchial relaxation, however, is less than that produced by epinephrin. Demerol probably has a theoretic advantage as an anti-asthmatic agent, they state, because it tends to reduce the autonomic reactions usually associated with a severe attack. Epinephrin may relieve the asthma but probably heightens the fear component. Good results have been obtained with a mixture consisting of 35 mg. of demerol and half the usual amount of epinephrin. Demerol is a synthetic product (1-methyl 4-phenylpiperidine 4-carboxylic acid ethyl ester hydrochloride).

Jimenez Diaz<sup>30</sup> "desensitized" three asthmatic patients with antitetanic serum. Three weeks after the first serum effect, intracutaneous test doses are given with 1:10,000 dilution of the serum. The concentration is then increased until reactions are provoked. The intracutaneous injections are then continued but with dilutions not strong enough to cause severe shock. [This procedure seems to be dangerous as severe anaphylactic shock seems not impossible.]

A number of papers have appeared in the field of inhalation therapy in bronchial asthma. Barach<sup>2</sup> treated twenty-six hospitalized and forty-five ambulatory patients who had intractable asthma by a routine aimed at producing repeated bronchial relaxation. If the spastically contracted circular bronchial muscles can be relaxed over a five- to ten-day period prolonged freedom from severe asthma should result. In the hospital the patients were given (1) rectal injections of 0.5 gm. of aminophyllin once or twice daily for a period of one to three weeks; (2) inhalation of helium-oxygen mixtures for one to six hours daily for five days; (3) dilaudid, generally in 2 mg. doses, in some cases, given rectally with aminophyllin; (4) potassium iodide 1 to 3 c.c. daily; and (5) inhalation of the nebulized spray of 1:100 epinephrin and in some instances of 1 per cent neosynephrin, one to five times daily. Hypodermic injections of epinephrin were used only if the inhalation method failed.



## PROGRESS IN ALLERGY

Ambulatory patients received potassium iodide, the spray of 1:100 epinephrin and rectal instillations of aminophyllin, followed by inhalation of helium-oxygen for one hour. Barach's results were good, although probably no better than obtained by most men who have not employed so meticulous a procedure. In 100 courses of therapy to these seventy-one patients, 57 per cent were either completely or almost completely relieved of symptoms, 25 per cent lost their refractoriness to epinephrin and were somewhat improved, and there was little or no improvement in 17 per cent. The duration of improvement varied from one week to more than a year. The prolonged rectal instillations of aminophyllin are especially valuable in asthmatics who also have emphysema, says Barach.

Lockey<sup>34</sup> added 5 per cent glycerin to 1:100 epinephrin used for inhalation. He divided sixty asthmatic patients into two equal groups. Of those who inhaled the glycerin-epinephrin mixture 82 per cent stated that irritation and dryness of the throat was markedly lessened as compared to these symptoms which frequently follow inhalation of epinephrin without glycerin. Westcott and Gillson<sup>65</sup> found an increase in vital capacity and lessening of symptoms in asthmatics who inhale 1:100 epinephrin. In the less severe cases the relief was equal to that obtained by injection of epinephrin, and none of the patients who inhaled the drug became epinephrin-fast. Lockey also found additional relief by postural drainage and by breathing exercises. A rather interesting though not too scientific report comes from the resuscitation branches of the Fire Departments of Chicago and Los Angeles and the United States Coast Guard.<sup>53</sup> The survey covered three years, beginning in 1940, and deals with cases of asphyxiation of all types, including asthma. There were fifty asthmatic patients in the three groups [a few of these might have been victims of cardiac asthma], with five deaths; breathing had entirely stopped in three of these latter when efforts at resuscitation were started. Cardiac disease was by far the largest single cause of death and the author was unable to decide whether mechanical or manual methods of resuscitation are preferable in these emergencies.

Engelhardt and Derbes<sup>36</sup> continue to condemn the use of iodized oil in the treatment of bronchial asthma. They summarized the previous literature and note that "cure" cannot be expected in more than 2 per cent. Against this are the dangers: acute iodism; iododermas; acute paroxysms of cough with possible massive collapse (authors note one such case); the possible presence of the oil in the lungs for years; the occasional occurrence of pneumonia after instillation of the oil. In addition death may occur if local anesthesia is used; five fatalities occurred at the Charity Hospital of New Orleans in cases in which cocaine or pontocaine were given. They conclude that "iodized poppyseed oil has no place in the treatment of bronchial asthma. Not only is it of little value therapeutically but the dangers attendant upon its use are such that, even when indicated diagnostically, great care must be exercised."

Hull, Balyeat and Chont<sup>27</sup> have a good article on the therapeutic value

## PROGRESS IN ALLERGY

of roentgen treatment in chronic asthma. They point out that previous investigators in this field have failed to consider fully the importance of infected accessory nasal sinuses as an etiologic and aggravating factor in severe cases. Most of their 1,529 patients, therefore, received roentgen therapy not only to the chest but also to these sinuses. They conclude that severe asthmatics in whom infection is also present can frequently be controlled by this method. Patients who lack this "infection" element are not benefited by radiation. The technique of choice is the "cross fire" method in which the dosage is concentrated over the greatest areas of the lungs where most of the bronchial tubes are distributed. Danger is slight if care is used. This method should be checked by others.

Gompertz<sup>23</sup> writes on the uses of the bronchoscope in the treatment of asthma. He points out that obstruction may be due to (1) spasm of bronchial muscles; (2) thickening of the walls of bronchi and bronchioles from edema, hyperplasia, hypertrophy and cellular infiltration; (3) secretion of thick tenacious mucus; (4) paradoxical collapse of bronchi during cough or expiration; and (5) a not infrequent localized stricture-like narrowing of a bronchus (previously described as bronchostenosis by Prickman and Moersch). Bronchoscopy helps by removing thick tenacious sputum or in aspirating large amounts of thinner secretion; it is especially valuable in removing plugs which may be the cause of atelectasis and even of massive collapse. Purer specimens for autogenous vaccines are also available. Bronchoscopy is of little value in typical allergic asthmatic patients sensitive to known allergens.

Miscall and Rovenstine<sup>40</sup> have a long and scholarly paper on the physiological basis for the surgical treatment of asthma. They divide bronchial asthma patients into two groups: (1) the allergic, for which the ordinary methods used by allergists are indicated, and (2) the infectious (chronic) for which they advocate surgery. They first block the nerves. If successful the results are temporary. They then remove the stellate, second, third and fourth thoracic ganglia. Their results were good. Temporary but good relief was obtained in forty-seven of sixty-one cases (78 per cent) in which only nerve blocking was done. Later twenty-one of these patients obtained complete relief of symptoms from removal of the ganglia. They stress the point that surgery should never be done unless nerve blocking has previously been successful.

Hurst,<sup>28</sup> in an article on asthma in childhood, believes that "every asthmatic patient can derive much benefit from good advice. He can be taught a way of life; how to avoid the exciting causes of his particular brand of asthma, how to control attacks he is unable to prevent, and, above all, how to be happy in spite of the bad luck of having been born with the asthma diathesis." [This philosophic advice is very good *provided* that the allergic management be not neglected.] Svevo<sup>35</sup> has a sound little article which explains the relaxation technique to the asthmatic. After the patient has learned how to exhale he proceeds with the second part of the treatment, i.e., the speech therapy based on the chewing method.

## PROGRESS IN ALLERGY

A number of more general articles have also appeared. Cooke<sup>10</sup> strongly advocates the cautious but continuous use of autogenous vaccines in the infectious group of asthma. Rackemann,<sup>48</sup> Ratner<sup>49</sup> and Weiner<sup>64</sup> correctly condemn the use of morphine in asthma, and Ratner does not recommend aminophyllin in children. Guido Ruiz Moreno<sup>41</sup> analyzes many of the non-specific measures used in therapy, including peptone; and the Sterlings<sup>57</sup> analyze 200 patients with chronic bronchial asthma.

Unger and Wolf,<sup>62</sup> in reporting the results of treatment in 459 cases of bronchial asthma during twenty years, found that of the 207 cases which had been previously discussed seven years ago results were for the most part still satisfactory; relapse was rare. An additional 252 asthmatic patients were listed and the cases were divided into paroxysmal and chronic groups. The best results were naturally obtained in the paroxysmal group, especially in those whose symptoms were due to a known allergen which could be eliminated and especially in those whose symptoms began in the first decade of life (144 out of 459). The need for early treatment was stressed, and prophylactic therapy in children, outlined. The mortality rate in the entire series was about 10 per cent (this included death from all causes); asthma was the chief cause of death in twenty-one cases and a contributing factor in another sixteen. The use of morphine in asthma is contraindicated as it may cause death by diminishing the ability to cough up the viscid sputum.

Moreno, Solari and Bachmann<sup>42</sup> studied 733 allergic patients in Buenos Aires. Of these 431 had asthma, 360 rhinopathies and forty-one urticaria. The best therapeutic results were in the nasal cases with 69.5 per cent "cured"; 62.1 per cent of the allergic asthmatics were "cured." Inhalants caused 50 per cent of the cases, foods 29.8 per cent, pollen 11.7 per cent, bacteria and mushrooms 8.5 per cent. House dust and feather dust are especially important and the authors also blame streptococci and staphylococci.

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## BREAD-MOLD PREVENTIVE CURES ATHLETE'S FOOT

Sodium propionate, a chemical now being used by many large baking companies to check the growth of mold in bread and cake, is an effective remedy for athlete's foot, ringworm and many other fungous infections, Dr. Edmund L. Keeney, of Baltimore, and Comdr. Edwin N. Broyles, of the Johns Hopkins Medical School now serving in the Navy, report. (*Bulletin of the Johns Hopkins Hospital.*)

The chemical is used in an ointment, as a powder and in a solution. Some of the fifty-five midshipmen at the U. S. Naval Academy who used the chemical for athlete's foot were cured in four weeks.

The remedy was equally effective in patients with ringworm of the scalp and of the skin, fungous infections of the ear, thrush and blacktongue due to a fungus.—*Science News Letter*, February 12, 1944.

ABSTRACTS

Pediatrics

PANEL DISCUSSION ON ALLERGY AND IMMUNOTHERAPY. Twelfth Annual Meeting of the American Academy of Pediatrics. *J. Pediat.*, 23:231, (Aug.) 1943.

Under the chairmanship of Dr. Bret Ratner, authorities in their fields gave brief reviews as follows:

Serum Sickness—Dr. W. T. Longcope

The Anamnestic Reaction—Dr. P. R. Cannon

Desensitization—Dr. J. L. Alexander

Allergic Reactions Resulting from Toxoids—Dr. J. A. Bigler

The publication provides in capsule form an authoritative and well presented discussion of the various subjects. J. G.

IDIOSYNCRASY TO MERCURY PREPARATIONS IN CHILDHOOD: REPORT OF TWO CASES OF REACTIONS TO AMMONIATED MERCURY OINTMENT 5 PER CENT AND MERCURY BICHLORIDE SOLUTION (1:4000). Gibel, H., and Kramer, B.: *Ann. J. Dis. Child.*, 66:155, (Aug.) 1943.

The value of the widespread use of mercury preparations in children is beyond question, since they have been used for many generations with few reports attesting to any harmful action. Reactions caused by locally applied mercury preparations are to be considered not as poisoning but as true idiosyncrasy. The authors report a case in a twenty-two months-old girl who was treated for impetigo with ammoniated mercury ointment 5 per cent. Eleven days following, she developed a severe generalized erythematous, morbilliform eruption diagnosed by one physician as measles and by another as scarlet fever. She was hospitalized, and in twenty-four days, the skin returned almost to normal.

A second case is reported of an infant fourteen months of age whose diapers were rinsed in bichloride of mercury solution (1:4000). After six days' use, there developed fever and a "diaper area" erythema and induration, with a generalized morbilliform rash in the less confluent areas, and a scarlatiniform rash in the more confluent areas. The skin returned to normal in about fourteen days. The authors point out that it is not unusual for a patient to be susceptible to one compound of mercury and not to another; and that the different types of reactions may depend upon the drug used. The interval between the application of the drug and the appearance of the eruption varies between one and twelve days. The treatment is symptomatic. Twelve cases of idiosyncrasy to ammoniated mercury ointment have been reported from 1883 to 1942. No case of death caused by the local application of a mercury preparation to the unbroken skin has been reported. J. G.

ETHYLENE DISULPHONATE IN THE TREATMENT OF ALLERGIC CHILDREN. Wasson, V. P.: *Arch. Pediat.*, 60:511, (Sept.) 1943.

The basis for the use of this preparation was a report by Bodman and Maisin (1940) to the effect that an abnormality of carbohydrate metabolism was the primary cause of the allergic state, being due to the absence in the body of certain catalysts of coenzymal activity. They found that ethylene disulfonate in vitro fulfilled the requirements of such a catalyst and discussed the effects of the intramuscular injection of this drug. The author treated twenty allergic children using twenty others as controls under approximately standard conditions. The author concludes that the treated group may have benefited sufficiently for the drug to deserve further study. The tabular comparison of treated and untreated cases, however, does not seem to warrant such optimism. J. G.



## PROGRESS IN ALLERGY

### RELATION OF THE DOSE OF ANTIGEN TO THE DEGREE OF ANAPHYLACTIC SHOCK IN DOGS. Dragstedt, Carl A.: *J. Immunol.*, 47:505, (Dec.) 1943.

In contrasting the behavior of sensitized animals with that of normal animals, the sensitivity is more important than the toxicity of the antigen. Two sensitive animals, however, show a decided variation in their response to an antigen. The author reports his observations on 240 dogs sensitized to horse serum and for whom shock dosages were varied. Severity of the reaction was recorded by the extent and duration of the blood pressure fall, recorded by cannulation of the common carotid artery. Results show 0-40 per cent of the dogs died within thirty minutes from serum dosages varying from 0.13-2.0 ml. No dose of antigen would surely kill any animal. Hence there is no progressive increase in the severity of the reactions with the increase in the dose; which is indicative of the presence of variation in the animals' susceptibility to desensitization.

L. J. H.

### FOLLOW-UP STUDIES OF PYLOROSPASM IN INFANCY. Salmi, T.: *Acta Paediatrica*, 38:271, 1941.

This is a general report on seventy-two cases observed in the University Children's Hospital of Helsinki, Finland. The cases include those of pyloric stenosis and ranged in age from five months to twenty-one years. Sixty infants and children were observed with special reference to cutaneous allergic manifestations (eczema, urticaria and strophulus) which occurred in one-third of these cases as compared with an incidence of the same conditions in one-quarter of a series of 100 control cases. (ABSTRACTOR'S NOTE: Strophulus is a rather inexact term to denote what we term lichen urticatus, a form of urticaria peculiar to infants and children of unknown origin which disappears spontaneously at puberty. It is apparently much more common in Finland than in this country.)

J. G.

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## Miscellaneous

### HUMAN PLASMA AND SERUM TOXICITY. State, David, and Levine, Milton: *J. Lab. & Clin. Med.*, 28:1786, (Dec.) 1943.

There are conflicting observations in the literature regarding the relative merits of plasma and serum. Reactions occur with both. The authors use group specific plasma. Patients who are sensitive to A and B plasma by skin test, also show positive skin test to purified substances of Witebsky. Reactions follow intravenous administration of either material. Individuals are usually sensitive to only one group specific substance. Patients with sensitivity to plasma do not necessarily have allergic history. No correlation exists between the amount of antibody in recipient and the sensitivity. Only those individuals in the blood group showing specific antibody are sensitive, though all with antibody are not sensitive. The severity of the reaction depends on the reacting material and on the condition of the patient. Epinephrine is used for relief of symptoms. Reactions may occur under anesthesia, as evidenced by presented case history. Pooling is not an assurance of preventing reactions. Factors other than A & B substances responsible for reactions are: allergens or reagins in plasma or serum, pyrogens and unknown immunologic factors. Illustrative cases are presented. Skin tests with plasma is a good method of indicating sensitivity and is an aid in prevention of reactions. Bibliography.

L. J. H.



## PROGRESS IN ALLERGY

### SYSTEMIC ALLERGIC REACTION INDUCED BY YELLOW FEVER VACCINE. Swartz, R. H.: *J. Lab. & Clin. Med.*, 28:1663, (Nov.) 1943.

The author reports an anaphylactic type of response to a single immunization injection of yellow fever vaccine in a patient sensitive to ragweed and chicken. The vaccine was proven to be the instigating agent. Evidence is offered to substantiate the statement that the reaginic fraction of yellow fever vaccine is related both to egg white and chicken meat; but more closely to the former than to the latter. It would appear that egg and chicken sensitivity by history of skin tests would suggest care in the giving of yellow fever vaccine.

L. J. H.

### ACQUIRED SENSITIVITY TO INJECTABLE LIVER EXTRACTS. Warburton, Ralph T.: *Ohio State M. J.*, 39:10, (Oct.) 1943.

A case report of acquired allergy to liver extract in a non-atopic individual has been observed. Following surgical removal of two-thirds of the stomach, the result of lymphosarcoma, and followed by a course of deep x-ray therapy, which contributed to the patient's poor state of health and moderate macrocytic anemia, he was given liver extract (Reticulogen-Lilly). He received this every three to four days for four injections, and then had no further liver extract for a period of three weeks. Following another injection he developed an allergic reaction characterized by general feeling of warmth, swelling of the lips and tongue, diffuse urticaria, itching of the palms of the hands and soles of the feet, palpitation, sense of pressure in the chest, asthmatic breathing. These symptoms lasted for a period of one hour, followed by marked state of exhaustion for three to four hours. In view of the fact that Reticulogen-Lilly contains 3.0 mg. Thiamine Chloride per c.c., the patient was tested with Thiamine Chloride to determine the question of a possible sensitivity. The test was negative after injecting 0.1 c.c. of 5 per cent solution intradermally. The patient was also tested with 1-1000 concentrations of liver extracts from other sources, including both pork and beef livers, and significant reactions were obtained to all such extracts. The author further attempted to sensitize another individual having an allergy to spring grasses following a comparable schedule as observed in the former patient; there was no evidence of sensitivity. It was also suggested by the author that, in addition to the anti-anemic principle, the vitamin fractions must be considered as allergic factors.

J. W. T.

### ROLE OF FOOD ALLERGY AND HYPERTENSION. Price, A. Sumner: *Rev. Gastro-enterol.*, 10:233, (Oct.) 1943.

The author feels that hypertension results from the accumulation of minor, subminor allergens; the first being those used two to three times a week, and the second, those used daily. Based upon Coca's work in non-reagenic food allergy, this allergy is said to be peculiar to the gastro-intestinal tracts with signs and symptoms referable to the secondary shock organs which varies from individual to individual. In hypertensive patients, the kidneys and vascular tree are involved. Sensitivity to vegetable protein occurs more commonly than does that of animal protein, although the latter when it does appear is usually more severe.

Six cases are presented in which a definite association between the ingestion of specific foods and hypertension could be demonstrated. The pulse rate was taken before eating, and thirty, sixty and ninety minutes post-prandial. A rise in blood pressure followed repeated consumption of allergen, but was occasionally delayed until the pulse returned to normal range. The author feels that little is to be gained clinically in cases which may be in the terminal phases of nephrosclerosis.

L. J. H.

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# Questions and Answers

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**Is the incidence of allergic reactions following transfusion of human blood plasma frequent?**

**Army M.D.**

Allergic reaction to plasma transfusion is relatively very low when one considers the enormous quantities now being used. When it does occur, however, it may be very serious or fatal.

In this connection it might be of interest to refer to an interesting report of a severe allergic reaction resulting from receiving blood plasma by a patient sensitive to ragweed. (W. J. Colonnell, U. S. Nav. Bull., 41: 1356, 1943). Dr. Colonnell reports a severe systemic reaction following the transfusion of an activated pooled blood plasma in a patient hospitalized for persistent intestinal bleeding. Two months prior this patient received whole blood from a type A donor, with no reaction. A month later he received another whole blood transfusion from the same donor, which was followed by a light urticaria relieved by epinephrine. Four weeks later, following the transfusion of about 175 c.c. of an activated pooled blood plasma, the skin became flushed, and there was conjunctival injection with lacrimation. The transfusion was stopped and 0.1 c.c. of a 1:1000 dilution of epinephrine was injected intravenously. There then developed periorbital and laryngeal edema and a marked generalized urticaria. An intramuscular injection of epinephrine did not prevent dysphagia, dyspnea, and dysphonia. There was marked edema of the uvula and soft palate. His chest revealed many musical râles. It was necessary to give another dose of epinephrine before the symptoms subsided.

The patient showed a 3 plus reaction to ragweed pollen and a 1 plus reaction to the plasma used on intradermal testing.

Passive transfer tests with blood from the patient prior to transfusion showed the presence of ragweed reagins.

Patients sensitive to ragweed as well as allergics not sensitive to ragweed and non-allergics were skin tested with the plasma used in this case and the evidence indicated the presence of ragweed allergen in the plasma.

Evidently the ragweed antibody was received by the whole blood transfusion, and the allergen by the plasma transfusion, which caused the allergic reaction.

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**What is the anesthetic of choice for an emergency operation when the patient is having bronchial asthma?**

**M.D., Colorado**

This question was referred to Dr. Ralph T. Knight, Professor, Director of Division of Anesthesia, University of Minnesota, for an answer. He states that cyclopropane is the anesthetic of choice and, if possible, some helium should be administered with it. The latter can be withdrawn as soon as the patient is anesthetized when the bronchial spasm has disappeared. However, one should be prepared to use the helium subsequently, if necessary. Cyclopropane is preferred because in the presence of a bronchial spasm, the anesthetist gets a chance to introduce more oxygen and this anesthetic stimulates the mucus secretion the least. Some use pentothal, but this depresses the respiration and there would be a tendency to get an insufficient respiratory exchange in the presence of asthma.

# Correspondence Items

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## Food Allergies and Vitamin C

To the Editor:

I read with interest in the *ANNALS OF ALLERGY*, Dr. Holmes' article on "Food Allergies and Vitamin C." In his paper he claims that he treated successfully twenty-five patients with hay fever by the daily administration of Vitamin C during the pollen season.

What I do not understand is the food allergies that he lists (e.g., milk, egg, wheat, et cetera) as causing hay fever. Does he mean that these foods caused vasomotor rhinitis which was mistaken for hay fever or secondly that these foods aggravated the pollen cases? It isn't likely that these foods bothered the patient only in the hay fever season and could be tolerated the rest of the year.

I have given eight patients 500 mgm. Vitamin C for several months. They were asthmatics chiefly affected by house dust and some foods. My results showed no improvements whatsoever.

On two patients I gave B and C vitamin capsules daily without any results. In one patient the B factor seemed to aggravate quiescent cholelithiasis.

I am not criticizing Dr. Holmes' work, I am only asking for more explanations. Heaven only knows that we allergists can use all the help we can get from any reliable source.

Please publish this letter because it might stimulate other men to report their results with Vitamin C.

Sincerely yours,

H. H. OBERFELD.

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## Toxic Allergenic Plants in Brazil

To the Editor:

In wartime every subject that concerns the welfare of soldiers is considered of vital importance, so, we thought it would be of interest to make some observations regarding the probable influence of our toxic-allergenic plants upon the health of the American soldiers, at present stationed here in Brazil.

Among the toxic-allergenic plants found in Brazil, the *Lithrea molleoides* (anacardeacea) is clinically the most important. This small tree contains a toxic-allergenic principle identical to that of the *Rhus*, and is widely distributed throughout our territory, from North to South. If the American soldiers are by chance exposed to it, many of them might be affected by the *Lithrea*.

From our four consecutive years of study on the atmospheric pollen content of many of the principal Brazilian cities, we came to the conclusion that there is only one pollen season of importance: the gramineae (grass) season. This season occurs from the middle of May to the middle of June and the daily amount of pollen per 1.8 sq. cm. is comparatively low. In four years of observation, the highest amount of pollen found in twenty-four hours of exposure was 160 grains. During the other months, the grass-pollen may be found, but in irregular and negligible quantities. The grass responsible for the May-June season is the *Melinis minutiflora* (capim gordura). It is distributed from latitude 17° to 25° approximately. Therefore, the cities of Northern Brazil (Natal, Recife, Belem) where the American sol-

## CORRESPONDENCE ITEMS

diers are at present concentrated are not subject to this season. But, in the vicinity of the city of Rio de Janeiro the *Melinis minutiflora* is very abundant.

The *Cynodon dactylon*, the *Hyparrhenia rufa*, the *Panicum maximum* are the other grasses most widely distributed in Brazil. They are, however, according to our observations, of less importance in pollinosis. Other allergenic plants in the United States (*Amrosiae*, *Gartneria*, *Iva*, *Xanthium*, *Artemisia*, *Acnida*, *Atriplex*, *Salsola*, *Plantago*, et cetera) are scarce or non-existent here.

Summary. Our anemophilous anthropocoreous plants do not satisfy the postulates set forth by Tommen, as they are too sparsely distributed (with exception of the *Melinis minutiflora*). Those plants, therefore, need not be considered as a possible cause of allergic symptoms found among the American soldiers stationed here in Brazil.

A. OLIVEIRA LIMA, M.D.  
J. B. GRECO, M.D.  
Brazil, S. A.

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### Contact Dermatitis Due to Permanent Wave Process

Recently we have seen three patients with contact dermatitis due to a "cold" or "heatless" permanent hair wave process, when products were used furnished by the Helen Curtis Company.

I have written to Dr. Louis Schwartz, Medical Director and Chief of the Dermatoses Section of the U. S. Public Health Service, for the formula and chemical data before reporting the details of these cases in a later communication.

RALPH BOWEN, M.D., Houston, Texas.

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We are pleased to acknowledge receiving the first monthly (May) issue of *Revista Argentino-Norte Americana de Ciencias Medical (Review of Medical Sciences of Argentine-North America)*, Ayacucho 576, Buenos Aires, Republica Argentina. It contains 143 pages with an imposing format, large readable type, and is profusely illustrated. Annual subscription price outside of Argentine 30 pesos (about \$6.25 present exchange). The magazine is edited by a large staff of eminent physicians representing the various departments of the Argentine Medical School. It contains an American Inter-University section representing the American Inter-University Bureau of the Faculty of Medical Sciences. The latter has been founded for the benefit of the American University fraternity "in order to keep alive and foster the ties of moral, scientific, teaching and administrative character between all and each of the Faculties and Schools of Medical Science of the American continent." There are thirteen scientific articles representing the various specialties, including one on allergy, and four by United States authors. Each article is summarized in English, and there is a college news section as well as an excellent book review department. The American College of Allergists, through its organ, the *ANNALS OF ALLERGY*, is very proud to be cooperative in those efforts which will in any way serve to promote a mutual understanding between the peoples who speak the two languages most widely spread throughout the world.—F.W.W.

# News Items

## HONORARY FELLOWS

Dr. Louis Schwartz, Medical Director, Chief, Dermatoses Section, U. S. Public Health Service, Bethesda, Maryland, and Dr. Bela Shick, 17 East 84th Street, New York, N. Y., have been elected Honorary Fellows of the College for their meritorious contributions to allergic research and high attainments in the science of allergy.

## FELLOWSHIP CERTIFICATES

The Honorary, Active, and Associate Fellowship certificates of membership are now being framed and most of the members will receive theirs, ready for hanging, by March 15. They will be mailed to the home address of those members who are abroad in the Service. Lack of personnel, supplies, and the influenza epidemic contributed to the delay.

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### ARGENTINA

Dr. Miguel Augustin Solari, Carlos Pellegrini 1219, Buenos Aires, has been elected a Corresponding Fellow of the College.

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### BRAZIL

Dr. J. B. Greco, Rua da Baia 1887, Belo Horizonte, Minas, Brazil, who has published valuable contributions on Allergy in journals published in Brazil as well as in this country, has qualified as an Active Fellow of the College.

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### CUBA

Dr. José Frederico Dumm, 55-406 La Plata, Brazil, has been elected a Corresponding Fellow of the College.

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Dr. José M. Quintero, Havana, formerly a Corresponding Fellow, has been elected an Active Fellow of the College.

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### SANTIAGO DE CHILE

Dr. E. Diaz Carrasco, who is a prominent allergist in Santiago de Chile, has qualified as an Active Fellow of the College. His address is Arturo Prat, 72.

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Dr. A. Oliveira Lima, Av. Rio Branco, 277, Rio de Janeiro, has been elected an Associate Fellow of the College.

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### PACIFIC COAST

Arrangements are being made by Fellows of the Pacific Coast area to organize a section of the College and to hold a regional meeting in the near future.

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### FIRST ANNUAL MEETING

The Board of Regents, as announced in the November-December issue of THE ANNALS, voted to hold the First Annual Meeting of the College at Chicago, June 10-11, 1944. With the official approval of the American Medical Association, arrangements have been completed with the Palmer House at Chicago, for College headquarters. Let us make it our duty to attend and participate in College activities in every manner.

The College, incorporated as a non-profit organization a little over a year ago, set forth in its charter certain aims and purposes which included among other plans, the establishment of an organization international in scope of qualified medical men and scientists who would meet at designated times for the purpose of promoting and advancing the study, research and clinical knowledge of allergy as



## NEWS ITEMS

it applied to the various specialties in medicine; to maintain and advance the highest possible standards among those engaged in the practice of allergy, as well as to promote friendly intercourse in the practice of allergy.

The purpose of the College is to give proper recognition to otolaryngologists, ophthalmologists, pediatricians, dermatologists, gastro-enterologists, as well as the internists who are applying allergy to their practice.

With these functions in mind, the Program Committee is developing plans to have Instructional Courses in Allergy as it applies to these various specialties, to be conducted by recognized leaders in their specialty. These courses, limited to applicants, will be intensive, lasting one hour each, two on Saturday morning, June 10, and two on Sunday morning, June 11, from 8:30 to 10:30. This arrangement makes it possible for members to attend all four courses, if they desire.

The remainder of Saturday morning will consist of a Symposium on "Allergy in Wartime," with three speakers representing the Army, the Navy and the United States Public Health Service speaking twenty-five to thirty minutes each. In addition, there will be three commentators of high scientific standing who will be allowed ten minutes each.

Saturday afternoon and Sunday morning, following the instructional periods, will be devoted to papers on Investigative and Clinical Allergy. Arrangements have been made for a luncheon meeting on Saturday and an informal dinner in the evening with entertainment.

Sunday afternoon will be devoted to meetings of the officers and various committees of the College, which will be followed by a business meeting of the entire College.

It is hoped that as many as possible will make hotel reservations, as well as arrangements for transportation to and from Chicago, at the earliest possible date. For a list of the Chicago hotels compiled by the Convention Bureau of the American Medical Association, as those cooperating with the A.M.A. for their June 1944 convention, see page 264 of the November-December issue of *THE ANNALS*.



### PROGRAM COMMITTEE FOR THE CHICAGO MEETING

The Program Committee for the Chicago meeting consists of the following members: Dr. Erich Urbach, Chairman; Dr. Jonathan Forman, Vice Chairman; Drs. David Pipes, W. P. Garver, Jerome Glaser, Michael Zeller, and Fred Wittich.

Physicians who would like to present papers at this meeting should write immediately to the Chairman, Vice Chairman, or to the Secretary of the College. Please send a brief résumé of the material which you would like to present at the meeting, not later than April 1, 1944.



### SCIENTIFIC EXHIBITS

Dr. Thomas C. Hull, Director of Scientific Exhibits for the American Medical Association, has supplied the Secretary of the College with applications for scientific exhibit space. Members of the College desiring to apply for this space should write to the Executive Offices of the College, at 401 La Salle Medical Building, Minneapolis, for an application. The Scientific Exhibit will be held in the Palmer House. The Technical Exhibit will be held under the auspices of the American Medical Association. For space, our advertisers should communicate with Mr. Will Braun, Business Manager, American Medical Association.



### THE ANNALS

*THE ANNALS* is being mailed to every member of the College both at home and abroad. Please notify promptly the Secretary of the College of any change of address. *THE ANNALS* hereafter is being mailed as first class matter to all members in the Armed Service here and abroad, in order to insure forwarding. When pre-

## NEWS ITEMS

viously sent as third class mail some members did not receive their copies because forwarding postage was required.

The Editorial Board will be pleased to receive items of interest from any allergist for publication in the News Section of the journal. Your friends, both here and abroad, would be pleased to hear from you. Mail such items to the College offices at Minneapolis.

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It is intended that the number of pages of THE ANNALS will not be increased for the duration or as long as there is a paper restriction. The publishers have been requested by the Government to conform to this restriction and also to use smaller type, when possible.

Grateful acknowledgment is made to those members of the Editorial Board of THE ANNALS who have so loyally contributed to the comprehensive reviews and abstracts of the literature on Allergy. THE ANNALS is now listed in the Cumulative Index.

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## GENERAL NEWS

The College Research Foundation is growing (see page 258 of the November-December issue). It is hoped that the honor roll can be announced at the Chicago meeting. It is a good investment. Send in your contribution now.

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The Southwest Forum for Allergy convenes April 15-16, Jackson, Mississippi. Headquarters: Robert E. Lee Hotel. For further details, write to: Dr. George Owens, 910 North State Street, Jackson, Mississippi.

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Dr. French K. Hansel of Saint Louis has been elected president and Dr. Orval Withers of Kansas City, vice president of the American College of Allergists by vote of the Board of Regents, to function until the first annual meeting next June. Major L. J. Halpin, M.C., has been elected a member of the Board.

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## CORRECTIONS

The following tabulation was inadvertently omitted from the article by Dr. Arthur F. Coca entitled "The Normal Adult Human Pulse-Rate" which appeared on Pages 212-218 in the November-December, 1943, issue. It should have appeared on page 213 following the words at the end of the first paragraph, reading, "with the results as shown in the accompanying tabulation."

	Lowest Count	Highest Count	Range
1	62	72	10
2	62	72	10
3	66	76	10
4	69	76	7
5	70	78	8
6	72	80	5
7	72	82	10
Average	68	76.5	9

\* \* \*

The first sentence in the abstract of the article by Dr. William F. Petersen on page 198 should read as follows:

"Although one environmental factor, such as meteorological changes, is seldom alone responsible for the varying degrees of organ function and dysfunction in the complex human mechanism, Dr. Petersen implores the specialist and practitioner to recognize this important factor in our environment."

## BOOK REVIEWS

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*Books listed here become the property of the College library when reviewed. A microfilm or miniature photostat service will be available to the members at cost. Members, however, are requested to write reviews on any book which may be of interest to allergists.*

**PSYCHOSOMATIC DIAGNOSIS.** By Flanders Dunbar, M.D. 750 pages. Price \$7.50. New York: Paul B. Hoeber, Inc., 1944.

Since psychosomatic medicine is rapidly being applied to all specialties and general medicine, there is no physician who will not receive much benefit from this comprehensive work.

The text represents the extensive investigative and clinical study of the subject during a period of twelve years at the Presbyterian Hospital, New York.

It is based on the records of over 1600 patients with cardiovascular disease, diabetes, fracture, gastrointestinal disease, and allergy, and presents both the physiological and psychological terms of these diseases. There are twelve chapters with important features such as the psychosomatic history, special techniques of examination, the hidden factors, case histories, personality profiles, therapy and the clinical and practical considerations.

—F. W. W.

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**HUMAN CONSTITUTION IN CLINICAL MEDICINE.** By George Draper, M.D., C. W. Dupertuis, Ph.D., and J. L. Caughey, Jr., M.D., Med. Sci.D. 273 Pages. 29 illus. Price \$4.00. New York: Paul B. Hoeber, Inc., Medical Book Department of Harper and Brothers, 1943.

The book contains twenty-four chapters and is a compendium for medical students who are interested in the relationship between individual human constitution and disease. The growing interest in psychophysiological phenomena gives proper significance to initial functional disturbances in their relation to chronic disease. The authors assumed a difficult task when preparing such an essay for the medical student. They stress the importance of taking, in addition to the patient's routine history of his symptoms, a biography of "his heritage, infancy and childhood experiences, growth and developmental phenomena, and his mode of response to every sort of experience which has befallen him."

The insight and satisfaction obtained when approaching the individual patient with some knowledge of the constitutional problem and the specific environmental stress in relation to the disease process warrants a close study of this work by every medical student who wishes to cultivate his talents.

This brief compendium is an admirable approach for all those who would understand the man within the patient.

—F. W. W.

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**PATHOLOGY AND THERAPY OF RHEUMATIC FEVER.** By Leopold Lichtwitz, M.D. 225 pages, 69 illus. Price \$4.75. New York: Grune and Stratton, Inc., 1943.

It was very unfortunate that Professor Lichtwitz did not live to see his manuscript in print, although a very able Foreword by Dr. William J. Maloney epitomizes the author's text.

Dr. Lichtwitz masterfully marshals convincing scientific and clinical evidence that the mechanism of allergy plays an important role in the etiology of rheumatic fever.

## BOOK REVIEWS

His interpretation and correlation of the clinical complexities of rheumatism with those of the puzzling symptom-complexes of allergy challenges investigators in both fields to offer convincing evidence otherwise.

The thirteen chapters completely comprise a classification and an analysis of the various types of rheumatic and arthritic affections. Dysfunctions and structural involvements are precisely detailed clinically.

The confused processes of rheumatic pathology are logically explained on the basis of a fault in the defensive mechanism due to an antigen-antibody reaction caused by various foreign proteins either exogenous or more often endogenous, such as from damaged tissue proteolysis and others from metabolites of invading microorganisms.

The book is compact, easily read, with numerous excellent illustrations of typical clinical types, including x-rays, and histopathology. The internist who is an allergist first can fully appreciate its value. However, its practicability warrants every practitioner's having it available.

F. W. W.

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DIAGNOSTIC VALUE OF CERTAIN SYMPTOMS OF MINOR ALLERGY  
(VALOR DIAGNOSTICO DE CIERTOS SINTOMAS DE ALERGIA  
MENOR). By Benigno R. Garat. Buenos Aires, Argentina: Libreria Hachette  
S. A., June 25, 1943.

This booklet of forty-one pages relates the statistical studies made by the author on the symptomatic manifestations of Allergy as found in the zone of the Federal Capital of Argentina. He states that the allergic diseases occupy a special position in pathology, because they are an expression of a diathesis, which can exist in certain periods of a person's life without manifesting any clinical symptoms, or without knowing that these symptoms are signs of disease. He adds, "To us minor allergy is really subclinical allergy."

The subclinical character is determined by these three factors: (a) by the infrequent contact with the excitant; (b) by the sparing clinical sensitivity; (c) by the little or limited alarming character of certain symptoms of hypersensitiveness.

Under Subclinical or Minor Allergy he includes the following: Minor coryza, seasonal or nonseasonal; cough; bronchial spasm; bronchorrhea; urticaria; the equivalent of eczema; contact dermatitis; sharp or pungent taste of the tongue and lingual symptoms of paresthesia; foul (gritty) tongue; minor bucal edema; ulcerations of the mouth; halitosis; sialorrhea (ptyalism); permanent congestion of the pharynx pyorrhea-simple gingivitis; regurgitations; pyrosis; gastric acidity; sensation of fullness; sensation of dilatation of the stomach; repetition of the taste of certain foods; eructations; sleepy feeling after meals; digestive embarrassment of children; nausea; anorexia; diarrhea; lientery (diarrhea with passage of undigested food) with constipation; constipation of specific form; proctorrhea; sensation of weight in the rectum and sensation of incomplete evacuation; hemorrhoidal crisis; and pruritus ani.

The conclusion of his studies made on 404 allergic and 100 nonallergic patients are as follows:

1. The respiratory forms are the most frequent ones. They figure two-thirds.
2. In the decreasing or descending order, follow the cutaneous eruptions (dermatoses), migraine and those of the digestive disturbances.
3. Urticaria is predominant in females and bronchial manifestations in males.
4. The cutaneous eruptions appear before the fifth year of life; the respiratory diseases after the age of five and hayfever and migraine after puberty.
5. Allergic manifestations appear isolated in only one-fifth of the cases.
6. The most frequent association is the respiratory form. It is noted, however, that the urticarias and the diarrheas appear in the first year of life.